ANNUAL SESSION · ATLANTIC CITY · JUNE 11-15, 1951

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# THE JOURNAL

OF THE

## American Medical Association

VOLUME 145, No. 5 • Subscription, $15.00
Single Copy, 45 Cents

Published Weekly at
535 North Dearborn Street, Chicago 10, Illinois

February 3, 1951

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THE JOURNAL of the American Medical Association is published weekly by the American Medical Association. Subscription price, $15.00 a year, 45c a copy. Canadian $16.50. Foreign $19.00. Entered as second class matter June 25, 1885, at the Postoffice at Chicago, Ill., under act of March 3, 1879. Address all communications to American Medical Association, 535 N. Dearborn St., Chicago 10, Illinois

# THE JOURNAL

## of the American Medical Association

*Published Under the Auspices of the Board of Trustees*

VOL. 145, NO. 5 — CHICAGO, ILLINOIS — FEBRUARY 3, 1951

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## THE TOXIC EFFECTS OF ANTIHISTAMINIC DRUGS

*J. B. Wyngaarden, M.D.*
*and*
*M. H. Seevers, M.D., Ann Arbor, Mich.*

During recent years we have witnessed the development of an increasing number of effective antihistaminic agents, whose role in the therapy of allergic disease has now become well established. Recently a great mass experiment has begun in the treatment of the common cold with these compounds, and striking claims have been made for the efficacy of their early administration. An avid public has been eagerly supplied by various manufacturers until at present the consumption of these agents is enormous. Reliable estimates are that the total sale of these drugs will reach $100,000,000 in 1950.[1]

Fortunately, the antihistaminic compounds have proved to be relatively nontoxic in the usual doses, though they do frequently give rise to bothersome side effects. There are, however, certain serious potentialities embodied in these agents, and a small number of deaths have occurred. It is our purpose in this report to call attention to the toxicity of antihistaminic agents, noting particularly the serious and fatal reactions from them. We will present a collected series of 11 cases of fatal intoxication, including two previously unreported cases, and will also discuss certain instances of serious reaction or great overdosage with recovery. The remarkable susceptibility of children to the convulsant action of antihistaminic agents will be stressed. Finally, some experimental toxicity and antidotal data will be briefly presented.[2]

### SIDE REACTIONS

The common side reactions of the various antihistaminic agents have been reviewed adequately[3] and will not be treated exhaustively here. A classification of the more important or unusual ones is given in table 1, in which the untoward reactions[4] are roughly grouped into seven systems: (1) nervous; (2) gastrointestinal; (3) cardiovascular; (4) respiratory; (5) genitourinary; (6) cutaneous and mucosal, and (7) hematological. The commoner reactions are drowsiness, sleepiness, dizziness, headache, insomnia, nervousness, nausea, vomiting, constipation, diarrhea, and dryness of the mouth. Different agents may possess these side effects to varying degrees; the incidence of side reactions ranges from 10 to 63 per cent or more in patients using various preparations. Certain agents may be prone to cause specific types of side reactions; e. g., diphenhydramine (benadryl®)[3c] causes predominantly central nervous system effects, and tripelennamine (pyribenzamine®) causes chiefly gastrointestinal symptoms.[4b'] It is important to note that a significant group of patients finds it necessary to discontinue the use of a particular preparation because of the severity of the side reactions. In one study[4b'] this group ranged from 6 to 16 per cent of the patients using one or another antihistaminic preparation. Claims of unusually low incidence of toxicity have been made for certain compounds.

The effects of antihistaminic drugs on mental efficiency have received recent attention. All 10 subjects of one study exhibited some impairment of mental processes while using the drugs.[4d'] A Navy project[4e'] concluded that the "toxic effects of benadryl® are such that the piloting of aircraft during the course of the drug's action may be hazardous." The effects of diphenhydramine on the central nervous system have been implicated as a contributing factor in an accident.[4c']

### FATAL REACTIONS

While we shall not minimize the common side effects discussed above, our present aim is to call attention to the more serious and, fortunately, far less common reactions caused by antihistaminic compounds. There have been a number of deaths from these agents,

From the Department of Pharmacology, University of Michigan Medical School.
Dr. Wyngaarden is presently located at Massachusetts General Hospital, Boston.

1. Antihistaminics for Colds, editorial, J. A. M. A. **142**: 570 (Feb. 25) 1950.

2. The cases reported herein have been collected by communication with manufacturers and distributors of various antihistaminic drugs and, in many instances, by communication with physicians acquainted with the patients involved. It is believed that this represents all of the known cases of fatal poisoning.

3. (*a*) Loew, E. R.: Pharmacology of Antihistamine Compounds, Physiol. Rev. **27**: 542-573 (Oct.) 1947. (*b*) Loveless, M. H.: Therapeutic and Side Effects of Pyribenzamine and Benadryl, Am. J. Med. **3**: 296-308 (Sept.) 1947. (*c*) Waldbott, G. L.: The Antihistaminic Drugs, J. A. M. A. **135**: 207-209 (Sept. 27) 1947. (*d*) Waldbott, G. L., and Young, M. I.: Antistine, Neoantergan, Neohetramine, Trimeton, Antihistaminique RP-3277—An Appraisal of Their Clinical Value, J. Allergy **19**: 313-316 (Sept.) 1948. (*e*) Spain, W. C., and Pflum, F. A.: An Evaluation of the Present Status of Antihistaminic Substances, New York State J. Med. **48**: 2272-2275 (Oct. 15) 1948. (*f*) Feinberg, S. M.: The Antihistamine Drugs, Pharmacology and Therapeutic Effects, Am. J. Med. **3**: 560-570 (Nov.) 1947. (*g*) Sacks, B. A.: The Toxicity of Benadryl: Report of a Case and Review of the Literature, Ann. Int. Med. **29**: 135-144 (July) 1948.

4. Because of lack of space these bibliographic references are omitted from THE JOURNAL; they will appear in the authors' reprints.

chiefly from accidental overdosage. Death may result in a variety of ways. Most striking is the susceptibility of children to the convulsive properties of those compounds which produce stimulating effects. Severe hyperthermia, cerebral edema and upper nephron nephrosis have also been observed in this age group. In adults convulsions are uncommon and depressant effects are more serious. Two deaths in depression have been reported, one of which is clearly related solely to the ingestion of an antihistaminic compound. One adult fatality from agranulocytosis has been reported in the lay press, and eight other recorded cases have been followed to recovery.

There have been at least eight fatalities in children under 2 years of age, five of which were accompanied with convulsions (table 2). In two other infants who died the cause of death was not stated, but judging from the short survival following ingestion and the pattern of other well described cases, convulsions may have been present. It appears that the latent period may be very short and that convulsions may begin in one-half to two hours following ingestion, preceded by signs of cerebral depression or of irritation.

TABLE 1.—*Acute Toxicity of Antihistaminic Agents in the Human*

I. Nervous system

A. Central

1. Stimulation
   - Insomnia
   - Nervousness
   - Vagal stimulation
   - Tachycardia and hypertension
   - Muscular twitchings
   - Hyperreflexia
   - Tremor
   - Convulsions

2. Depression
   - Drowsiness
   - Somnolence
   - Narcolepsy
   - Weakness
   - Ataxia
   - Delirium
   - Coma

3. Neuropsychiatric
   - Nightmares
   - Impaired judgment
   - Delusions
   - Hallucinations
   - Mental depressions
   - Reduced mental efficiency
   - Confusion
   - Toxic psychosis

4. Miscellaneous
   - Dizziness
   - Headache
   - Syncope
   - Fever
   - Hyperthermia
   - Cerebral edema
   - Electroencephalographic changes

B. Peripheral
   - Toxic neuritis
   - Paresthesias
   - Paralysis
   - Areflexia

C. Special sense organs

1. Ears
   - Tinnitis
   - Vertigo
   - Labyrinthitis

2. Eyes
   - Dilated pupils
   - Blurring of vision

II. Gastrointestinal system
   - Anorexia, nausea and vomiting
   - Heartburn
   - Cardiospasm
   - Diarrhea
   - Constipation

III. Cardiovascular system
   - Hypotension
   - Vasovagal phenomena
   - Syncope
   - Shocklike state
   - Palpitation
   - Tachycardia
   - Hypertension
   - Cerebral edema
   - Electrocardiographic changes

IV. Respiratory system
   - Asthma

V. Genitourinary system
   - Irritative symptoms
   - Spasmogenic retention
   - Upper nephron nephrosis

VI. Skin and mucous membranes
   - Dry mouth
   - Dermatitis
   - Urticaria

VII. Hematological system
   - Neutropenia
   - Agranulocytosis
   - Hemolytic anemia

Convulsions are of the intermittent clonic-tonic type, at times accompanied with threshing movements of the limbs. The pupils are characteristically dilated and fixed. Deepening coma ensues. Cardiorespiratory depression may supervene, with apnea, cyanosis and vascular collapse. Deaths have occurred in two to 15 hours after ingestion.

In two fatal cases there was hyperthermia above 107 F. In one of them [4m] acute renal failure was also present, but hyperthermia and cerebral edema appear to have been the chief causes of death, which occurred 15 hours after the ingestion of only 100 mg. of methapyrilene (thenylene®) hydrochloride. Renal shutdown of such short duration would not commonly be fatal. In the second child [4p] the sequence of events clearly

TABLE 2.—*Fatalities from Antihistaminic Agents in Infants*

| Age, Yr. | Sex | Weight, Lb. | Drug | Dose, Mg. | Major Effect |
|---|---|---|---|---|---|
| ½ | .. | .. | Diphenhydramine hydrochloride | ? | Died in convulsions 2 hours after ingestion |
| 1¼ | .. | 25 | Antergan® | 1,500 | Died 6 hours after ingestion |
| 1½ | F | .. | Methapyrilene hydrochloride | 100 | Died 15 hours after ingestion; hyperpyrexia, cerebral edema, upper nephron nephrosis, uremia |
| 1⅝ | F | .. | Pyranisamine (Neoantergan®) maleate | 600 | Died 2¾ hours after ingestion; posteonvulsive coma |
| 1⅝ | M | .. | Dimenhydrinate | 700(?) | Died in convulsions and coma 4½ hours after ingestion |
| 1 11/12 | .. | .. | Antergan® | "10 tablets" | Died 6 hours after ingestion |
| 2 | F | .. | Pyranisamine hydrochloride | 1,400 | Died in convulsions 4 hours after ingestion |
| 2 | M | 27 | Diphenhydramine hydrochloride | 474 | Died in convulsions, coma and hyperpyrexia 13 hours after ingestion |

excludes fever per se as the cause of the convulsions, and they must in this case be attributed to diphenhydramine.

Two previously unreported cases of fatalities in children from the ingestion of antihistaminic agents are included in this report.

CASE 1.[4j]—A 6 month old infant consumed an unknown quantity of diphenhydramine on March 25, 1948. He was examined soon after by a physician, who found nothing seriously wrong and did not prescribe treatment. An hour later the child became violently ill and was rushed to the hospital in convulsions. Death occurred 10 minutes after arrival, about two hours after ingestion of the diphenhydramine.

CASE 2.[4k]—A 22 month old boy who had been in good health except for a mild upper respiratory tract infection was brought to a physician about two hours after the alleged ingestion of seven 100 mg. tablets of dimenhydrinate (dramamine). The child initially exhibited hyperexcitability, and later generalized convulsions and a diffuse erythema of the skin developed. Despite gastric lavage, intramuscular injections of sodium phenobarbital, intravenous injections of Hartman's solution, calcium gluconate and nikethamide and eventually artificial respiration and intravenous injections of epinephrine, the child died. Terminally he was cyanotic and his rectal temperature was 101 F. Death occurred 4½ hours after ingestion of the dimenhydrinate.

Postmortem examination revealed severe fresh hemorrhages of the lungs, diffuse in the lower lobes and focal in the upper lobes. There was mild to moderate polymorphonuclear reaction in the hemorrhagic areas, appearing to be secondary to the hemorrhage. There was moderate interstitial pneumonitis in nonhemorrhagic portions of the lung. The brain was markedly swollen and microscopically showed tiny fresh hemorrhages and intracellular edema. There was diffuse hyperplasia of lymphoid tissue in the lymph nodes, small intestine, spleen and thymus. The remainder of the organs were free of pathological changes.

The pathological findings in this case are too extensive to be attributed to the mild pneumonia and hence must be considered as due to the dimenhydrinate, either as a direct toxic effect or partially as an indirect change resulting from anoxia.

The three adult fatalities occurred from central nervous system or bone marrow depression. One teenaged girl died of the depressant effects of 1,500 mg. of diphenhydramine hydrochloride taken in a successful suicidal attempt.[46r] A 47 year old severely asthmatic woman died in depression after ingesting only 200 mg. of diphenhydramine hydrochloride.[41r] A 65 year old man died of agranulocytosis resulting from the use of an antihistaminic agent.[42r] The latter fatality probably represents an idiosyncratic reaction, although details of this case are not yet available. The death of the asthmatic woman, however, cannot be unequivocally attributed to diphenhydramine, since the shocklike state observed could well have been a complication of the disease itself and may have been influenced by other depressant medicaments given. The cases of toxicity in this review resulted from accident, ignorance, suicidal intent, impaired judgment caused by the drug itself [47r] or iatrogenic causes.

## NONFATAL EXCESSIVE INGESTION

The number of instances of recovery from excessive doses of antihistaminic agents is slightly greater than the number of deaths (table 3). Starr and Rankin [49] record the case of an 18 month old infant who ingested from 150 to 250 mg. of diphenhydramine hydrochloride, went into convulsions one-half hour later, and recovered in 24 hours after treatment of the seizures with magnesium sulfate, phenobarbital and amobarbital (amytal®). Snyderman [47r] described a 20 month old boy who ingested 800 mg. of methapyrilene hydrochloride and began to have convulsions one hour later. Fluids by the parenteral route, phenobarbital, sodium bromide and chloral hydrate were employed, and the child recovered and left the hospital 48 hours after admission. These are, however, the only known cases of recovery from convulsions caused by the antihistaminic drugs in children under the age of 2 years.

Beyond the age of 2 years, several cases of nonfatal ingestion of large doses have occurred, in some with serious and alarming reactions and in others with very minimal signs of toxicity. The susceptibility of children to the convulsant action of antihistaminic agents is striking and impressive. The ability to withstand large overdoses appears to increase with age, and the older the patient the more does the toxic manifestation shift from that of central nervous system stimulation to that of depression. Convulsions can, however, occur in the adult. Noteworthy also is the great variation in tolerance of excessive doses, a difference not entirely due to inherent potency variations. A group of cases will emphasize these points.

CASE 3.[45]—A girl between 2½ and 3 years of age was found in a drowsy, listless, fretful state. She became disorientated and walked with a staggering, awkward gait. Jerkings of the extremities developed, and then she experienced generalized clonic convulsions. One and one-half hours earlier she had been playing in a bathroom from which 17 capsules of diphenhydramine hydrochloride (850 mg.) were later found to be missing. About five hours after probable ingestion gastric lavage was carried out. She was then treated with fluids intravenously, phenobarbital subcutaneously (160 mg. over six to eight hours) and oxygen. There were recurrent generalized convulsions for about eight hours; the face was flushed, and the pupils were dilated and nearly fixed. Between seizures the child cried out and talked in a rambling manner and showed hyperextension of the trunk and involuntary movements of the extremities. The next day she appeared normal. The gastric washings, later analyzed by Parke, Davis & Company, revealed diphenhydramine-like organic bases. Over the next two years she remained well and no sequelae were noted.

CASE 4.[48r]—In 1947 a 32 month old baby swallowed 9 capsules (450 mg.) of diphenhydramine hydrochloride, after which a state of excitation was observed. Phenobarbital was prescribed, and the next day the baby was well.

CASE 5.[48]—On June 8, 1947 a man interned in an army disciplinary barracks ingested 2,500 mg. of diphenhydramine hydrochloride with suicidal intent. In about 12 minutes he became drowsy, and about 35 minutes after ingestion he was found in a comatose condition. Gastric lavage was promptly performed, and a portion of the drug was recovered. He was transferred to Oliver General Hospital, Augusta, Ga., and was received in coma, though reactive to external stimuli. The pupils were dilated and fixed. Respirations were full and blowing. The blood pressure was 185/120, and the pulse was full and of normal rate. Petit mal seizures of the left side of the face were observed.

For about 62 hours he remained irrational, highly excited and semicomatose. No specific therapy was given. On regaining consciousness he noted complete paralysis of both lower extremities associated with subjective "sleeping sensations." On his fourth hospital day he was seen by a neurologist, who found deep and superficial reflexes to be absent, sensation moderately impaired and profound weakness. These signs disappeared over the next five days, and recovery was complete except for some hysterical overlay giving slight weakness of the right leg and sensory loss of the right hand. It was felt that he had initially had a toxic neuritis or radiculitis. (Neuritic symptoms have previously been noted as a manifestation of toxicity from diphenhydramine.[43r]) Extensive laboratory

TABLE 3.—*Nonfatal Excessive Ingestion of Antihistaminic Agents*

| Age, Yr. | Sex | Weight, Lb. | Drug | Dose, Mg. | Effect |
|---|---|---|---|---|---|
| 1½ | M | 22 | Diphenhydramine hydrochloride | 150-250 | Convulsions |
| 1⅝ | M | .. | Methapyrilene hydrochloride | 800 | Convulsions |
| 2½ | F | .. | Diphenhydramine hydrochloride | 850 | Convulsions |
| 2⅝ | .. | .. | Diphenhydramine hydrochloride | 450 | Excitation * |
| 3 | F | 30 | Diphenhydramine hydrochloride | 700-800 | Convulsions |
| 3½ | M | 33 | Diphenhydramine hydrochloride | 100 for 2 days; 200 mg. on 3rd day | Epileptiform movements |
| 4 | M | 36 | Prophenpyridamine | 175 | Toxic psychosis |
| 18 | F | Obese | Diphenhydramine hydrochloride | 2,000(?) in 48 hr. | Affection of judgment |
| 20 | F | .. | Dimenhydrinate | 1,200 | Lethargy, somnolence |
| 21 | F | .. | Dimenhydrinate<br>Hydrillin<br>Aspirin | 22 tablets<br>50 tablets<br>50(?) tablets | Nervous system irritability and hyperpnea |
| 23 | F | 133 | Prophenpyridamine | 1,500 | Toxic psychosis |
| 28 | M | .. | Diphenhydramine hydrochloride | 1,500 in 60 hr. | Toxic psychosis |
| Adult | M | .. | Diphenhydramine hydrochloride | 1,500 | Coma; petit mal seizures; toxic neuritis |
| Adult | F | .. | Methapyrilene hydrochloride | 1,000 | Stimulation; convulsion |
| Adult | .. | .. | Chlorprophenpyridamine maleate | 400 (100 tablets) | No serious effect |
| 39 | F | .. | Tripelennamine hydrochloride | 1,350 in 48 hr. | Tonic contracture; cardiorespiratory collapse |
| 40 | F | 140 | Methapyrilene hydrochloride | 800 in 12 hr. | Convulsion |
| 72 | M | 145 | Diphenhydramine hydrochloride | 2,500 | Somnolence |

* Pinkus, H.: Personal communication to E. C. Vonder Heide, Parke, Davis & Company.

studies revealed no evidence of hematological, hepatic, renal or carbohydrate metabolism derangement.

CASE 6.[4v]—A woman took 1,000 mg. of methapyrilene (histadyl®) hydrochloride orally with suicidal intent. She became very much stimulated, alert and anxious, and when a physician attempted to pass a stomach tube a convulsion resulted. She recovered without further treatment.

CASE 7.[4x]—One evening in 1946 a 72 year old asthmatic man, weighing 145 pounds (65.8 Kg.), consumed 2,500 mg. (50 capsules) of diphenhydramine hydrochloride. The next morning his wife was unable to rouse him from a deep sleep, but that afternoon he was feeling well and walking in the park, free of asthma. He had received no medication for his somnolism.

CASE 8.[5]—A young woman, in her twenties, was seen by a physician at her home because of extreme lethargy. It was learned that she had ingested 12 tablets (1,200 mg.) of dimenhydrinate, and 100 mg. of phenobarbital. She was taken to a hospital in a stuporous and lethargic state, though she was not seriously ill. Picrotoxin (3 mg.) and later aminophylline (250 mg.) and some amphetamine sulfate were given; 2½ hours later the family insisted on taking the patient home. It was felt that she would probably have recovered without any treatment.

CASE 9.[6]—A Minnesota patient ingested 100 tablets (400 mg.) of chlorprophenpyridamine maleate (chlor-trimeton maleate®) with no serious effects.

Whiting[7] has observed a 21 year old woman who ingested 50 hydryllin (diphenhydramine and aminophylline) tablets, 22 dimenhydrinate tablets and about 50 acetylsalicylic acid tablets with suicidal intent. Approximately half of the total amount was recovered by lavage. She was initially unconscious, with exaggerated reflexes, dilated pupils and hyperpnea. Toxicity appeared to be due chiefly to salicylate overingestion, and with restoration of bicarbonate equilibrium she made an early recovery.

The study of Bryant,[4w] in which he gave methapyriline hydrochloride to adult manic-depressive patients in doses up to 1,400 mg. per 24 hours for six days, or up to 13,200 mg. in 13 days, also demonstrates the extraordinary tolerance of certain patients for certain antihistaminic compounds. However, in one patient, a 40 year old woman weighing 140 pounds (63.5 Kg.) a severe convulsion occurred following the administration of 800 mg. of methapyriline hydrochloride in a 12 hour period.

## UNUSUAL REACTIONS

There have been a number of rather bizarre reactions noted from the antihistaminic agents in average doses. Peculiar idiosyncrasies may on occasion lead to unusual and profound reactions, such as delirium,[4z] narcolepsy,[4y] shocklike states,[4g', r'] labyrinthitis,[4o'] cardiospasm,[4n'] urinary retention,[4q', 4a'] fever,[4a', k'] syncope[4o, y] and dermatitis.[8] These bizarre reactions are thought to be commoner in allergic persons.[41] Indeed, certain persons have manifested allergic reactions, such as asthma[2c, g] and contact eczema,[4n', t'] to the antihistaminic agents themselves. A case of arthralgia and urticaria following the use of thonzylamine (neohetramine®) has been called to our attention. Whether this can properly be attributed to the drug rather than to the antecedent infection is, of course, open to some doubt, since the type of sensitization phenomenon described can follow streptococcic infections. The possibility exists, however, that it was related to the drug, and the case is therefore mentioned briefly.

CASE 10.[4u']—A 43 year old man took 200 mg. of thonzylamine hydrochloride over a 16 hour period for a cold. Two days later pain developed in the right foot, followed in 12 hours by urticaria over the trunk, which spread during the next three days to involve 75 per cent of the body. These signs were associated with painful swelling of several joints. After 16 days of treatment with ephedrine, amobarbitol, calcium ascorbate and calamine lotion he made an uneventful recovery. He gave no previous allergic history, but he had been subject to migraine headaches.

Most previously reported cases of serious toxicity concern ingested drugs. Contact allergies[4n, t'] and intravenous toxicity studies[4g] have, however, been reported for certain compounds. Two cases of convulsions following unusual routes of administration of antihistaminic agents have recently been related to us, although in the second case the causative agent may conceivably not be the antihistaminic drug.

CASE 11.[4v]—A 6 year old child with a generalized allergic dermatitis was brought to the hospital. The intern first gave an injection of epinephrine, without effect. He then injected 100 mg. of methapyrilene hydrochloride intravenously, after which the child had a convulsion. The child recovered, and the dermatitis promptly improved.

CASE 12.[4v]—A patient with a severe burn covering most of the trunk was brought to a hospital. A large amount of lotion of methapyrilene and of cyclomethycaine (surfacaine, Lilly) was applied, and one to two hours later the patient had a convulsion. He recovered without ill effects. (Cyclomethycaine in L.D.$_{50}$ doses may cause muscular contractions experimentally.)

## EXPERIMENTAL TOXICITY

Virtually all the antihistaminic agents produce convulsive or postconvulsive depressant deaths in laboratory animals. Mice, rats, rabbits, guinea pigs, dogs and cats have given qualitatively similar responses to toxic doses. Primary depressant signs are minimal in these animals.[3] Chronic administration is usually well tolerated, though some visceral changes are occasionally noted.[9]

We undertook to study the acute effects of diphenhydramine and tripellenamine in the Macacus rhesus monkey to determine whether depressant reactions could be produced, or whether results would conform to those of smaller animals and to the pattern of toxicity in small infants. Fifteen monkeys weighing 2.8 to 5.3 kg. were used in 22 experiments, and then killed, since tuberculosis had been found in the colony. The drugs were injected subcutaneously in 5 to 10 per cent solutions. With sufficient doses of either compound, progressive hyperexcitability, tremors, spasmodic jerkings and clonic-tonic convulsions occurred regularly. Early death might result from the convulsions or, if these were survived, from postconvulsive respiratory depression. In all cases of death the heart was noted to beat some minutes after respiration had

5. Winter, I. C.: Personal communication to the authors.
6. Wittich, F. W.: Personal communication to W. A. Wright.
7. Whiting, E. G.: California & West. M., to be published; personal communication to the authors.
8. Waldbott,[2c] Friedlander and Friedlander.[4o] Sulzberger, Baer and Levin.[4n'] Rattner and Graffin.[4o'] Strauss.[41']
9. (*a*) Gruhzit, O. M., and Fiskin, R. A.: A Toxicologic Study of Two Histamine Antagonists of the Benzhydril Alkamine Ether Group, J. Pharmacol. & Exper. Therap. **89**: 227-233 (March) 1947. (*b*) Vander Brook, M. J.; Olson, K. J.; Richmond, M. T., and Kuizenga, M. H.: Pharmacology of a New Antihistamine, β-Pyrrolidine-Ethyl-Phenothiazine (Pyrrolazote), J. Pharmacol. & Exper. Therap. **94**: 197-208 (Oct.) 1948.

ceased. Approximate $L.D._{50}$ values for subcutaneous administration in the monkey are these: diphenhydramine hydrochloride, 100 mg. per kilogram; tripelennamine hydrochloride, 35 to 45 mg. per kilogram. A few primary depressant and ataxic signs were observed from diphenhydramine in nonlethal doses (50 to 100 mg. per kilogram) but not from tripelennamine.

## TREATMENT

The treatment of convulsions from antihistaminic agents occurring in infants and children has been none too successful, particularly in those under 2 years of age. A few of the older children have survived convulsant reactions with little or no treatment. Others with mild seizures have been treated successfully with small doses of sedatives and hypnotics. Secobarbital (seconal®) [4b] and phenobarbital [10] have been used effectively. Magnesium sulfate, oral administration of phenobarbital and intravenous injections of amobarbital proved efficacious in saving one infant with severe convulsions.[4q] Duerfeldt [4t] employed dihydromorphinone (dilaudid®) with partial success but finally resorted to the rectal administration of ether to gain control. He avoided barbiturates and other narcotics because of the attendant respiratory depression. Snyderman [4r] utilized phenobarbital, sodium bromide and chloral hydrate in the successful treatment of a 20 month old infant with convulsions from methapyriline.

In experimental convulsions in the monkey we found intravenous injections of thiopental sodium valuable, producing almost immediate cessation of convulsions. The smallest effective doses (about 5 to 10 mg. per kilogram) repeated as necessary seemed most advantageous. When the postconvulsive depressant phase began to predominate, respiratory stimulants were given with success. Caffeine, 10 mg. per kilogram intramuscularly, and ephedrine sulfate, 5 to 10 mg. per kilogram subcutaneously, were helpful.

It was found that cautious titration with thiopental was essential, since too small a dose allowed early recurrence of convulsions and too large a dose contributed to the depressant phase. The convulsions caused by diphenhydramine persisted, in some instances for nearly 24 hours. Excessive doses of stimulants fostered recurrences of convulsions. It was possible, however, by judicious use of the stimulants to prevent death in many instances at dose levels ordinarily fatal, but not when massive overdoses had been administered. It appears that with very large doses of either antihistaminic agent, particularly with tripelennamine, the mere control of convulsions is not effective in preventing death, which often occurs from deepening coma despite the administration of stimulants. In a 2 year old child suffering from convulsions, coma and cyanosis as a result of diphenhydramine ingestion, Davis and Hunt [4p] found that thiopental produced relaxation, with return of pupils to normal, without any real improvement in the patient's condition. It has previously been noted [9n] that pretreatment of rats with barbiturates will prevent convulsions from diphenhydramine, but will not alter the subsequent mortality rate of toxic doses of that drug. Our experience with the monkey is consistent with these observations.

Mephenesin (myanesin) protected the animal temporarily but not so effectively as thiopental. Other short-acting barbiturates might have been equally effective. Nikethamide was valueless as a respiratory stimulant in doses of 50 to 100 mg. per kilogram intramuscularly. Amphetamine was not used but would merit evaluation.

## COMMENT

On the basis of this review we have classified the toxic effects of antihistaminic agents as presented in table 1. The most important affection is that of the central nervous system. Children seem predisposed toward development of convulsions from toxic doses, adults toward development of depressant effects. However, convulsions have occurred in adults from large overdoses. Also, Churchill and Gammon [4j] have showed that diphenhydramine and tripelennamine may increase the abnormality of the electroencephalogram in adult epileptics and may even induce seizures. They caution regarding the use of antihistaminic preparations by epileptics. Several antihistaminic drugs have been shown to alter normal electroencephalograms.[4d] It is possible that quantities of these agents sufficient to cause convulsions can be absorbed through the broken skin.[4v]

The occasional occurrence of syncope and of vasomotor collapse represents another potentially serious effect of these agents. All antihistaminic agents are said to give vasovagal phenomena, such as ventricular depression, bradycardia, and transient vasodepression.[4f] Electrocardiographic changes have been noted in normal persons after the intravenous administration of rather large doses of diphenhydramine,[4g] and in two persons with heart disease after the ingestion of phenindamine (thephorin®).[4d] These changes were reversible.

Smooth muscle stimulation from those agents having the R-N-C-C-N = structure has long been recognized in animals. A few interesting human idiosyncrasies of this type have been reported, such as cardiospasm and urinary retention.[4q'] The constipation commonly experienced is another example of the spasmogenic activity of these compounds.

An atropine-like type of reaction has been described by Waldman and Pelner [4h'] in two patients with toxic delirium, dry mouth, fever, and mydriasis following prophenpyridamine (trimeton®) ingestion. They suggest the use of neostigmine in the therapy of this type of reaction, but in the one case in which it was employed its effect is difficult to evaluate. Certain of the reactions commonly observed from other agents also resemble this type of effect, and clarification of this point is needed. The abolition by thiopental of the pupillary dilatation caused by diphenhydramine [4p] would suggest that this effect was a direct central action of the antihistaminic drugs rather than a peripheral atropine-like action. At present the mechanism of toxic reactions has not been satisfactorily explained.

Three cases of hemolytic anemia from antihistaminic agents have been described, two resulting from diphenhydramine and one from tripelennamine.[4a''']

10. Gay.[4s] Winter.[5]

A rare but serious reaction is that of agranulocytosis. Nine cases have been reported,[11] only one of which has been fatal.[4m] As was pointed out by Drake,[4j] the compounds implicated in these reactions all contain a chemical unit closely related to the benzamine linkage present in aminopyrine, the notorious neutropenic agent of two decades ago, from which Kracke [12] singled out this group as the probable offender. Agranulocytosis has been reported in patients from 13 to 81 years of age, following three to eight weeks of antihistaminic therapy, from methaphenilene (diatrin®) hydrochloride, antergan® (dimethylamino-ethyl-benzylamine), or tripelennamine.[13] The first two agents named contain the benzamine linkage; the latter, the closely related alpha-pyridylamine group. This type of complex is notably absent from diphenhydramine and from many other antihistaminic compounds, but generalizations regarding agranulocytic potentialities of all members of this series would be hazardous on the basis of such tentative correlation.

It does not necessarily follow that the propensity to cause serious or fatal reactions is equally inherent in all compounds of this growing series merely because we have treated them here as a group. However, the type of toxicity encountered with all is similar, and the differences observed and discussed here may be in part artifactual, owing to greater experience with certain of the compounds. Experience does allow the assumption that several antihistaminic agents are capable of causing convulsive deaths in children, and judging from experimental data one should expect other agents to be equally capable of producing such reactions under similar circumstances. It is likely that the intensity of adult responses to overdoses will bear some relationship to the depressant potency of the preparation ingested.

The therapy of these serious reactions depends, of course, on the type of reaction encountered. In any event, use of the responsible agent should be stopped at once. Therapy must at present be entirely symptomatic, since a specific antidote is lacking. Histamine is not indicated, since the toxic effects of antihistaminic agents are in no way related to their antihistaminic activity per se. Whether use of histamine would be dangerous, as for example in collapse states, is not known, though one would reason that an overdose of an antihistaminic agent would afford considerable protection against the pharmacological actions of histamine. In one case in which it was tried, histamine did not suppress the convulsions caused by diphenhydramine and, indeed, produced asthmatic breathing despite the large overdose of the antihistaminic drug.[4t] The use of neostigmine for those reactions resembling atropine intoxication will bear evaluation.

In agranulocytosis the therapy is that of the disease, the scope of which is beyond this paper and well outlined elsewhere. In acute overdosage lavage is indicated immediately. Emetics, such as apomorphine, are to be avoided because of secondary respiratory depression. In convulsive reactions the short-acting barbiturates in repeated small doses may be helpful. Ether may be indicated and, indeed, deserves further evaluation, particularly so since respiratory depression is less marked with this agent than with the barbiturates. It would seem preferable to avoid long-acting barbiturates and narcotics because of the summation of late respiratory depressant effects. However, the somewhat specific anticonvulsant effect of phenobarbital may be useful, perhaps at times more so than the hypnotic and depressant effects of other barbiturates and thiobarbiturates. Stimulants during the depressant phase should be employed to assist respiration primarily, and thus caffeine, ephedrine and probably amphetamine would be useful, as well as oxygen and artificial respiration when needed.

It is important to recognize the range of toxicity of these compounds (table 1), particularly in view of their widespread and often unsupervised use today. While, fortunately, the serious and fatal reactions have thus far been few, they are likely to continue, especially where carelessness abounds. Susceptible patients and those with illnesses such as epilepsy and myocardial disease which may predispose them to possible untoward reactions should be given these agents cautiously. Children should be given these drugs only under the supervision of a physician, and excessive ingestion should be rigorously guarded against. Ideally, patients using these agents continually should have hematological checks periodically during their early experience with them. Medical supervision of the dispensing of these agents would certainly be preferable to the open traffic which today exists.

## SUMMARY

The common side effects of the antihistaminic agents have been tabulated and briefly commented on. Most of them are relatively innocuous and are important merely because they are annoying to patients. However, certain patients do avoid these agents because of the unpleasantness or severity of side effects.

Severe toxicity from these compounds is rare, but serious reactions have resulted from idiosyncracy or from overdosage. Twelve previously unreported cases of toxicity are presented, seven of them convulsive, two of them occurring in adults. Eleven fatal cases are reviewed, in eight of which the patients were children under the age of two years. Two of these cases were previously unreported. Infants and children seem predisposed to development of convulsions from overdoses, and the mortality rate in infants in whom convulsions develop is very high. Adults tend to development of central nervous system depression, which may on occasion be lethal. Agranulocytosis is another serious development, which has been reported nine times with one death.

The treatment of these reactions is purely symptomatic at present. Some suggestions as to therapy, based on successfully treated cases and on experimental observations, are offered. It is imperative that physicians be aware of the potential hazard of the antihistaminic compounds, as well as of their great usefulness. Fortunately, reactions thus far have been rare.

11. Clement and Godlewski,[4p] Blanton and Owens,[4n] Cahan, Meilman and Jacobson,[4s] Drake,[4j] Glassmire,[4r] Van Loon and Kanters,[4b] Hilker,[4o] Martland and Guck.[4d]

12. Kracke, R. R., and Parker, F. P.: The Relationship of Drug Therapy to Agranulocytosis, J. A. M. A. **105**: 960-966 (Sept. 21) 1935.

13. Blanton and Owens,[4n] Cahan, Meilman, and Jacobson,[4s] Hilker,[4o] Martland and Guck.[4d]

# BENIGN OBSTRUCTION OF THE LOWER ESOPHAGUS

*Nathan A. Womack, M.D.*
*E. S. Brintnall, M.D.*
*and*
*J. L. Ehrenhaft, M.D., Iowa City*

This report has to do with a relatively recent series of patients with benign obstructions of the lower esophagus all fundamentally of motor origin. Most of the patients have had the disease for a long time and have had many types of nonsurgical care. Often, therefore, when they have presented themselves for surgical treatment secondary complications of a morphological nature have been present, such as inflammation, ulceration, dilatation, recent scar formation and severe malnutrition. As evidence of the frequency and the importance of this condition, we shall report our experience with 23 patients who have been referred to the State University of Iowa hospitals for surgical care in a period of slightly over two years. The fact that the patients have come from a relatively limited geographic area of more or less the same genetic stock with a relatively similar environmental situation lends homogeneity to the group. We shall not, however, have long term follow-up studies. In our experience with this condition this is not too important, as most of the postoperative difficulties which we have encountered, as a rule, have been observed within a very short time after operation. With the passage of time, most of these patients have shown progressive improvement rather than deterioration. This also has been our experience with other patients treated for this condition who have been followed over a period of many years and who have not been included in this series.

This relatively common lesion has received considerable attention from surgeons in times past. It will be unnecessary to review the historical background, as this has been done most ably by Ochsner and DeBakey up to and including the year 1940 [1] and by others since then.[2]

## NORMAL MOTION

Because of the fact that the symptoms presented by these patients have to do with the motor mechanism of the esophagus, a brief review of the normal movements of this viscus is necessary in order that the proper interpretation be placed on the abnormality seen. This information is not easily obtained because the movements of the esophagus are either very fast or very slow. Much of the knowledge has come from inference drawn from the way the particular muscle encountered usually functions. Animal experimentation also has been of great help, although in this field much care must be used because of the variability seen in different species. The most important findings, and also those most difficult to interpret, have come from the observations made on the human esophagus by means of a fluoroscope.

It has been generally stated that the upper third of the human esophagus is composed of striated muscle; the middle third, of a mixture of striated and smooth muscle, and the lower third, entirely of smooth muscle. In studies that are going on in our department of surgery, which will be reported on in greater detail elsewhere by Dr. Rex Vaubel, we have found that, for the most part, this is true. There are many exceptions, however, and most of these are situations in which the striated muscle is relatively deficient, extending down only a few centimeters below the cricopharyngeus muscle. In the average person the striated muscle begins to be replaced by smooth muscle well above the superior level of the arch of the aorta and only a few strands are encountered below the level of the inferior surface of the aortic arch. When one recalls the basic differences in the movements of striated and smooth muscle, this transition has a potentiality of being an important factor in esophageal function. When the nerve supply to striated muscle is interfered with, it not only becomes incapable of contraction but loses its tonus as well. This is not true of smooth muscle. Furthermore, the speed of contraction of striated muscle is much greater than that of smooth muscle. It also is highly unlikely that striated muscle undergoes peristaltic movements in the classic sense, each wave of contraction being preceded by a wave of relaxation. What seems to be a peristaltic wave in the upper esophagus, thus, is probably a progressive series of rapid segmental contractions extraordinarily well timed. In the experimental animal with a musculature like that of the human, the cat for instance, when the nerve supply to this segment of the esophagus is cut, atony with subsequent dilatation results. Even when the muscle is stimulated directly, no peristaltic wave can pass along it. On the other hand, if the nerve supply is left intact and a considerable area of the striated muscle badly damaged the apparent peristaltic wave continues in an uninterrupted manner.

The lower portion of the esophagus functions in a manner similar to that of the small bowel, and the peristaltic wave can be propagated even though all apparent external nerve supply has been destroyed. The action of those striated fibers intermingled with smooth muscle can only be speculated on. It is possible that they may serve for the focal point of the beginning of the so-called secondary peristaltic wave that begins, as a rule, at about the level of the aortic arch and follows esophageal distention. These secondary waves play an important role in the emptying of the esophagus after the initial primary wave, which

From the Department of Surgery, State University of Iowa College of Medicine.

Read in the General Scientific Meetings at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 27, 1950.

1. Ochsner, A., and DeBakey, M.: Surgical Considerations of Achalasia, Arch. Surg. **41**: 1146, 1940.

2. Barlow, D.: Cardiospasm, Brit. J. Surg. **29**: 415, 1942. Vinson, P. P.: Cardiospasm, Am. J. Surg. **56**: 79, 1942. Faulkner, W. B., Jr.: Observations of Emotional Influence on Esophagus, J. Nerv. & Ment. Dis. **93**: 713, 1941. Eggers, C.: Cardiospasm, Ann. Surg. **115**: 215, 1942. Clagett, O. T.; Moersch, H. J., and Fischer, A.: Esophagogastrostomy, Surg., Gynec. & Obst. **81**: 440, 1945. Scott, W. J. M.: Idiopathic Dilatation of the Esophagus, Ann. Surg. **122**: 582, 1945. Lehmann, G.: Cardiospasm in Dog, Am. J. Physiol. **143**: 163, 1945. Schelbel, H. M.: Treatment of Achalasia, Surgery **20**: 558, 1946. Bell, H. G.: Cardiospasm—Treatment by Esophagogastrostomy, ibid. **20**: 104, 1946. Grimson, K. S.; Reeves, R. J.; Trent, J. C., and Wilson, A. D.: The Treatment of Patients with Achalasia by Esophagogastrostomy, ibid. **20**: 94, 1946. Petersen, F.: Transpleural Esophagogastrostomy, Tr. West. S. A. **52**: 108, 1946. Sweet, R. H.: Idiopathic Dilatation of Esophagus, S. Clin. North America **27**: 1128, 1947.

seems to be continuous with a contraction of the pharyngeal constrictors.

After the initial swallow, food accumulates in the esophagus until these secondary peristaltic waves, which have their origin in the region of the aortic arch, pass down to the cardia, emptying the esophagus in a milking fashion. Because of pharmacologic evidence and some morphological evidence, it is assumed that this secondary peristaltic wave has its adequacy dependent on the integrity of the ganglions of Auerbach. When these secondary waves are absent, adequate emptying of the esophagus generally is difficult. Normal peristaltic movement also can be interfered with by an area of tonicity too great to be overcome by the antecedent wave of relaxation. This is not infrequently seen in the lower portion of the esophagus and apparently can result from a local stimulus to the mucosa and muscle, as from inflammation or regurgitation of gastric juice, or from nervous mediation, either from cephalic stimuli or from stimuli arising from other viscera, such as is seen in periods of emotional stress or in associated lesions, such as duodenal ulcer.

Rarely in the lower portion of the normal esophagus focal areas of tonic uncoordinated contraction may be seen. These become of greater significance in the pathological state, when they are markedly exaggerated at times, even resembling diverticula. More commonly the picture is that of deep irregular serrations. It is most unusual to see such contractions in the relatively young person, and both in the normal and in the exaggerated state it is an observation made most commonly in the seventh and eighth decades of life.

When such esophageal movements as have been described above are considered objectively and descriptively, their coordination becomes a most complicated process. When the underlying biochemical phenomena of muscle contraction are better understood, however, this may possibly become simplified. For instance, it is highly probable that the contraction of smooth muscle may be to a considerable extent similar to that of cardiac and skeletal muscle in that it depends on the activation of the protein system of actomyosin by adenosinetriphosphate and that this is at least largely activated and controlled by the release of acetylcholine. In times past it was felt by some that this release of acetylcholine was entirely the function of the motor end plate. More recent work, which has been reviewed by Burn,[3] presents evidence that points to the synthesis of acetylcholine in the muscle wall as well, and therefore, as being independent of nerve structures. One can therefore speculate on the possibility that these numerous variants in esophageal motility that so often produce failure of normal emptying of the esophagus may be related fundamentally to the elaboration locally of acetylcholine, with its stimulatory and inhibitory effects. Such a concept would tend to explain the temporary beneficient effects that have resulted from the destroying or the anesthetizing of the extrinsic sympathetic nerve supply or the use of drugs of the atropine type. It also would tend to fit in with the recent general theory proposed by Burn that such medicinal agents as meperidine (demerol®) and diphenhydramine (benadryl®) may exert their effects by competing with the local hormonal action of acetylcholine, histamine and epinephrine.

However, until more fundamental light is shed on the subject, surgeons must limit their therapy for such functional obstruction to the utilization of the powerful primary wave of contraction brought about chiefly by the action of the strong pharyngeal constrictors. This can best be done by neutralizing the action of a considerable portion of the terminal esophagus by section of the circular muscle. This will relieve the patient of the damaging effects that result from increased tonus or contracture or inability of a peristaltic wave to traverse a particular area. Although we realize that eventually it may be shown that a single biochemical phenomenon may produce all the variants of esophageal obstruction of a functional nature, we feel that at the present time it is of considerable clinical value to divide them into several categories as related to the clinical conditions observed.

### CLASSIFICATION

A working classification that we have found to be of value is the following:

1. Paralysis or weakness of the striated muscle of the upper esophageal segment
2. Failure of peristalsis in the lower esophageal segments from
   a. Hypothetical ganglionic degeneration
   b. Abnormal tonus of psychic origin
   c. Increased muscle tonus or contracture due to regurgitation of gastric juice or to ulcer
3. Abnormal local functionless contractions, seen most frequently in the aged
4. Recovery or persistence of the primary cause with morphologic alterations such as
   a. Diffuse hypertrophy of the smooth muscle
   b. Esophagitis with or without ulceration
   c. Scarring

Lesions falling in the first category are relatively rare clinically, and there are no patients in our series who present pure weakness of the striated muscle segment. As has been stated, it can be produced experimentally by section of the vagal fibers supplying this segment. Such weakness has been reported in the human after diphtheria and scarlet fever. However, we have encountered it in times past in cases in which the patient presented no demonstrable antecedent etiological factor. It is possible that it may play a considerable part in the formation of the so-called megaesophagus, since often the massive dilation begins in the upper segment, the smooth muscle dilation coming on at a later stage.

By far the commonest cause of failure of the esophagus to empty in the series of cases that we are presenting falls in the second group, in which there has been noted a failure of normal peristalsis in the middle, and particularly in the lower, esophageal segment. We feel that it is unwise to include the conditions of all these patients under the general term achalasia, just as it is unwise to classify them all as being due to cardiospasm.

3. Burn, J. H.: Relation of Motor and Inhibitor Effects of Local Hormones, Physiol. Rev. 30: 177, 1950.

Templeton [4] has reecntly described fluoroscopic observations in which he noted that the primary wave of contraction, instead of proceeding the entire length of the esophagus, appeared to cease at about the level of the superior margin of the aortic arch. He noted that the portion of the esophagus over which the wave passed remained contracted for a second or two, after which this area relaxed and the contents of the esophagus flowed upward but were prevented from entering the pharynx by the contracted cricopharyngeus muscle. Secondary waves were not observed. In most of the patients he noted shallow segmental contractions of the lower segment that were purposeless and appeared and disappeared at different levels of the esophagus. Some of these waves produced an undulating effect for an area of a few centimeters but were never strong enough to move the bolus along and simulated the tertiary movement seen in the normal aged person. These undulating movements also were accompanied with generalized tonic contractions which diffusely narrowed the esophageal lumen. As this occurred, the barium mixture was forced into the stomach, the cricopharyngeus muscle remaining contracted.

In keeping with such fluoroscopic observations, we have noted that at operation on patients with this lesion the terminal esophagus for an area of 8 to 10 cm. appears to be in a state of tonic contraction. When mild faradic stimulation is applied to the muscle in this region, it undergoes little or no change, the change observed consisting chiefly in an increase in the generalized tonus. In the normal esophagus when such electrical stimulation is applied in this area, there is a brief moment of spasm which persists for two to three seconds, after which there is relaxation and a strong peristaltic wave originating at the point of stimulation and passing continuously down to the stomach.

Rake [5] and others have observed that the esophageal wall in this type of lesion presents relatively few ganglions of Auerbach and have suggested that the lack of normal peristalsis in this area is due to a failure of coordination of the smooth muscle fibers as a result of the absence of this ganglionic influence. This is an interesting concept but one that is difficult to prove. Such ganglions normally are scant in this area. Furthermore, many of these patients are in a poor state of nutrition and may show ganglionic degeneration secondary to thiamine deficiency. There certainly seem to be instances in which psychogenic factors play a role, and there is an unusually large group of such patients in the series on which we are here reporting. Furthermore, we have seen the identical picture present when there is a demonstrable ulcer of the peptic type in the lower esophagus and also when there has been a continuation of gastric mucosa into the terminal portion of the esophagus, with the subsequent irritating action of gastric juice.

The third type of lesion, that of abnormal local functionless contractions so often seen in the aged, is also rather rare. We have one such instance in this series. These patients can frequently be carried along satisfactorily with medical care and with large doses of atropine and diphenhydramine. Their nutritional state, as a rule, does not become nearly so precarious as does that of patients in the first two groups.

The morphological complications often noted in patients with long-standing lesions add greatly to the difficulty of adequate surgical care. Massive hypertrophy of the smooth muscle from the level of the lower margin of the aortic arch down to the stomach has been noted on two occasions. In both of these instances the esophageal musculature measured approximately 1 cm. in thickness, and the hypertrophy was present both in the circular and in the longitudinal fibers. Hypertrophy to a less degree and in a more localized area is more frequently encountered just above the entrance of the esophagus into the stomach. When there is much inflammation or ulceration or when the scarring is extensive, the ability to do the adequate plastic repair often is interfered with. In such cases esophageal resection must be resorted to.

*Summary of Results*

| Case | Age | Sex | Type of Lesion | Operation | Result |
|---|---|---|---|---|---|
| 1 | 72 | M | 2 | U-esophagoplasty | Good |
| 2 | 64 | M | 2 | Vagotomy; sympathetic denervation | Good |
| 3 | 31 | M | 4 | Resection | Good |
| 4 | 79 | F | 2 | U-esophagoplasty | Good |
| 5 | 75 | M | 4 | Resection | Good |
| 6 | 78 | M | 2 | Manual dilations | No improvement |
| 7 | 20 | F | 1 & 2 | U-esophagoplasty | Good |
| 8 | 34 | M | 2 | Manual dilation | No improvement |
| 9 | 48 | F | 4 | Resection | Good |
| 10 | 58 | M | 2 | Resection | Good after one dilation |
| 11 | 30 | M | 4 | Resection | Good after one dilation |
| 12 | 67 | M | 2 | U-esophagoplasty | No obstruction but probable marginal ulcer |
| 13 | 64 | M | 2 | Resection; followed by esophagoplasty | Good after second operation |
| 14 | 17 | F | 4 | Resection; followed by stenosis; later wide resection | Good after more extensive resection |
| 15 | 55 | M | 2 | Resection | Poor |
| 16 | 45 | M | 2 | U-esophagoplasty with secondary marginal ulcer; resection | Occasional bleeding from marginal ulcer |
| 17 | 53 | M | 2 | U-esophagoplasty | Good |
| 18 | 33 | F | 1 & 2 | U-esophagoplasty | Good |
| 19 | 12 | M | 4 | Resection | Requires dilation |
| 20 | 64 | F | 2 | Resection | Good |
| 21 | 40 | F | 2 | U-esophagoplasty | Good |
| 22 | 28 | M | 2 | U-esophagoplasty | Good |
| 23 | .. | M | 3 | No operation | No improvement |

## CLINICAL OBSERVATIONS

This syndrome is no respecter of age, being seen frequently at all decades of life. In this series our youngest patient was 12 years old and our oldest 79. Males are more frequently subject to this condition than females, and this experience is no exception, as there were 16 males to seven females. The most commonly noted symptom was dysphagia, and, contrary to the statements often made, the difficulty in swallowing solid foods was much greater than that with liquids. Indeed, most patients were able to take liquids in some form except for relatively brief intervals. One would expect such dietary difficulties to be associated with weight loss, and this has been true, varying

4. Templeton, F. E.: Movements of Esophagus in Presence of Cardiospasm, Gastroenterology **10**: 96, 1948.

5. Rake, G. W.: Pathology of Achalasia of the Cardia, Guy's Hosp. Rep. **77**: 141, 1927.

from 15 to 85 pounds (6.8 to 38.6 Kg.). Because of the difficulty in swallowing heavy foods, a lack of protein is often evident. Vitamin insufficiencies, particularly of the B group, are often apparent. In one of our patients, there was considerable fatty infiltration in the liver, with early cirrhosis, splenomegaly and beginning portal hypertension. The symptom third in frequency was that of regurgitation of retained esophageal contents. This was present in most of the patients with severe lesions and was a cause of bitter complaint. Retrosternal pain, often of a disabling nature, was present in approximately half of the patients. Bleeding

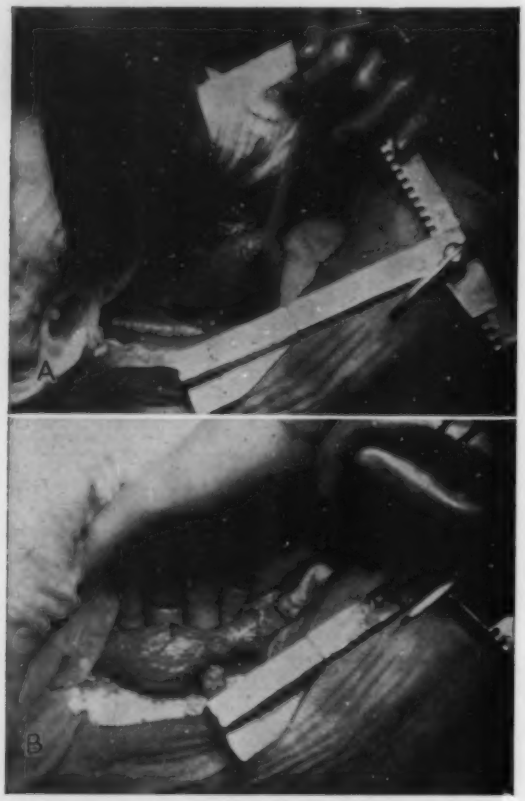


Fig. 1.—*A*, appearan.e of esophagus at operation, illustrating dilatation of upper and middle segments. *B*, Site of functional obstruction, extending at least 10 cm. from the cardiac orifice.

was occasionally encountered, particularly in those patients who presented evidence of ulceration or severe esophagitis. In only two patients, however, was this of severe consequence.

We were particularly interested in the emotional state of these patients, since there are many who would prefer to consider all variants of this syndrome under the general pattern of psychosomatic disability. A careful psychiatric history, therefore, was obtained on all patients. Where there was indication, expert psychiatric consultation was requested. Seven of the group were found to be emotionally unstable, but their instability was relatively mild in character. Six were considered to show classic evidence of psychoneurosis. Ten of the 23 patients were considered to be normal so far as their emotional reactions were concerned.

We were interested in the appearance of concomitant lesions, particularly in the abdominal viscera. Except in two patients with mild cholecystitis, neither of whom had a clinical history of the disease, no other important lesions were noted.

In seven of these patients it was possible to insert a nasal tube through the obstruction into the stomach for gastric analysis. The results were normal in terms of both night secretion and response to histamine in five patients but distinctly increased in two. Interestingly, both the latter patients presented a classic old peptic ulcer of the esophagus.

When the patients in this series are grouped under the categories mentioned above, we find that two of them presented weakness of the upper striated muscle with early megaesophagus. There were 15 who showed a failure of normal peristalsis in the lower esophageal segment. In four of these we were able to demonstrate frank ulceration. In the remaining 11 the failure of peristalsis could have been due either to an

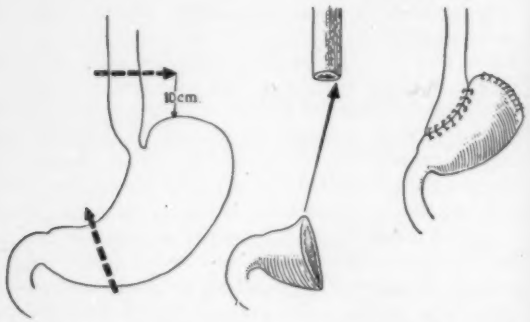


Fig. 2.—When resection is indicated, the acid-secreting portion of the stomach must be removed to prevent marginal ulceration. Note the method of esophageal anastomosis.

abnormal tonus of psychic origin or to the possible failure of ganglionic function. Morphologic studies could not be done on these patients to demonstrate such a lesion because of the inablity to secure adequate tissue with safety to the patient.

In one patient there were multiple focal areas of tonic contraction of a functionless nature producing obstruction. Another, in whom there was in all probability psychogenic origin of the increased tonus, showed tremendous hypertrophy of the smooth muscle extending from just below the aortic arch down to the stomach. Near the distal portion of the stomach during crises of pain, a pseudodiverticulum could be identified, probably representing a focal area of smooth muscle atony. In five of the patients there was severe inflammation or stricture formation, although a moderate degree of edema and inflammation was encountered in the terminal esophagus in practically all patients whose condition had been of long standing.

## TREATMENT

All these patients had received considerable medical care before consulting us. This consisted of the use of antispasmodic drugs, barbiturates, frequent

feedings with a soft or liquid diet and, in several instances, psychotherapy. Ten patients had had previous treatments by esophageal dilation, either with bags or with bougies.

Two patients, for significant reasons, were treated by a gastrotomy with manual dilation of the terminal esophagus through an abdominal appoach. Within four months both of these patients had returned with their original symptoms and with no change in their roentgenograms.

One patient who had a small limited area of what obviously was spasm just medial to the esophageal orifice and who had a clinical history suggestive of gastric regurgitation was treated by destroying the nerve

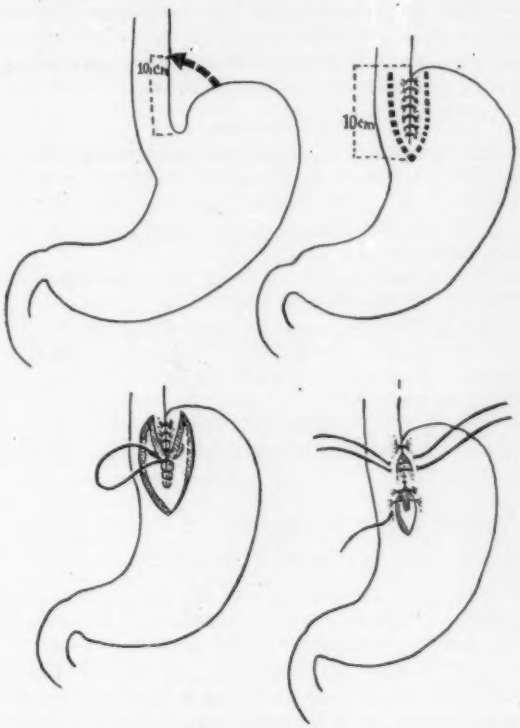


Fig. 3.—This type of plastic repair makes it possible to interrupt all that portion of the circular musculature of the esophagus that may be involved in the obstructive process.

supply to this local area, as well as by vagotomy. Interestingly, he has remained symptom free, and one year after operation his esophagrams are normal.

In 10 of the patients the degree of stenosis and the presence of considerable active inflammation and ulceration led to the choice of resection of the terminal esophagus. Three of these have had excellent results on a regular diet and have gained considerably in weight. Three others showed roentgenologic evidence of constriction at the anastomotic line but have responded well to one series of dilations. Two patients note a mild degree of postoperative dysphagia but have not considered it severe enough to submit to the discomfort of esophageal dilation. Finally, in two of these 10 patients marginal ulceration developed in the esophagus just above the anastomotic line, with scarring and ulceration producing practically complete stenosis.

It is obvious that marginal ulceration and inflammation following resection of the cardia present a serious and disabling complication. It became necessary, therefore, for us to modify the technic of our operation from that generally done in malignant disease where such complications are rare. In order to prevent the presence of acid-secreting tissue adjacent the esophageal mucosa, it has been necessary to do a most extensive resection of the stomach, removing all of the acid-secreting mucosa. In the normal stomach or in the stomach in which there is an increase in the secretion of acid, it is necessary that this resection be carried to the antrum. In older people in whom there is considerable gastric atrophy, this extensive a resection usually is not necessary. As has been demonstrated by Berger,[6] in most stomachs in which there is atrophy or any great degree of pathological disorder there is a tendency toward regression of the lower histological

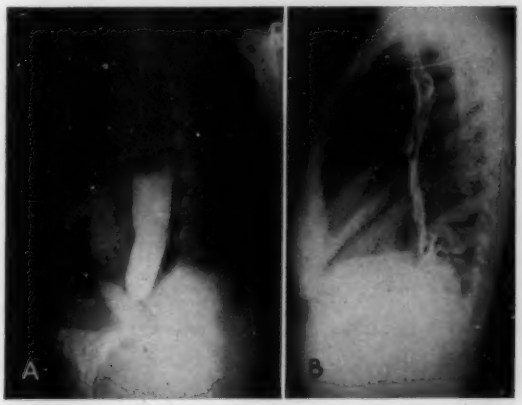


Fig. 4.—Roentgenograms before (*A*) and after (*B*) plastic repair as described in figure 3.

boundary of the body of the stomach or of that area occupied by the body glands. It, therefore, is possible in this operation to leave most of the lesser curvature, and in performing the end to side anastomosis the esophagus is sectioned obliquely producing a spatulate shape and thus decreasing the chance of spasm with resulting ischemia. We have found this technic of resection on the whole to be satisfactory. Our chief criticism would be that the small size of the residual stomach creates a feeding problem for several weeks until the patient can adjust his eating habits.

In those patients in whom there has been only a slight degree of inflammation of the terminal esophagus and in whom the chief difficulty has been a failure of normal peristalsis in the lower esophageal segment, we have elected to perform the "U" type of esophagoplasty. There have been nine such patients, and in all of them the results have been excellent. In two of

6. Berger, E. H.: The Distribution of Parietal Cells in the Stomach, Am. J. Anat. 51:87, 1934.

them, however, stool examination showed definite evidence of a transient period of bleeding in spite of the fact that there was no history of dysphagia or dyspepsia of any sort. We, therefore, are inclined to think that, in spite of the fact that these patients are relatively free from symptoms, one must always bear in mind the possibility of peptic ulceration.

This operation has been described in considerable detail in a previous communication by one of us.[7] In it the fundus of the stomach is brought up alongside the lateral wall of the esophagus and sutured in place. The incision then is carried down the terminal esophagus around the cardia and up the fundic portion of the stomach, the two mucosas brought together and, finally, the anterior layer of the stomach wall sutured to the anterior layer of the esophageal wall. This procedure resembles that type of pyloroplasty suggested years ago by Finney. Although in our previous experience this operation presented a considerable amount of relief from the dysphagia, many patients still found that it was necessary for them to eat slowly and roentgenogram films showed that there was a considerable amount of esophageal lag in emptying. In this series of patients we have utilized a transthoracic approach, sectioning the diaphragm and thus making it possible for us to have a minimum of 10 cm. of the terminal esophagus for our incision. This has made it possible for us to ablate most of the offending circular muscle of the esophagus, and we have been pleased to notice the relatively normal emptying of the esophagus after this more extensive procedure has been employed.

In the patient in our series who presented the multiple focal areas of tonic contraction in the lower esophagus, we felt it inadvisable to perform surgery. In all of the others, with the exception of the two in whom manual dilation was performed, the esophagus and stomach were approached transthoracically by removing the left eighth rib. We found that this approach gave better visualization and produced less operative shock. Three of our patients were over the age of 70 years. There were no postoperative complications other than than those which have been previously described, and there were no deaths.

### COMMENT

We feel that it is well to stress the fact that the area of musculature involved in the production of symptoms in this syndrome is often fairly extensive. Rarely, indeed, is it limited to the small commissure in the region of the cardiac orifice, and for this reason it usually is necessary to make a long incision through this musculature in the esophageal wall. In cases in our experience in which this has been done not only has normal emptying of the esophagus taken place but the roentgenographic deformities also have disappeared. The surgical approach, therefore, must be directed at the ablation of as much of the circular musculature of the esophagus as seems to be involved in the production of the emptying difficulties. Whether the surgical procedure is one of esophagoplasty or whether it is one of resection will depend on the individual situation. The provision of an additional stoma between the esophagus and stomach by a lateral anastomosis, as a rule, is not effective.[8] Apparently, the stoma too frequently becomes stenosed in a way similar to what happens when too much of the acid-secreting portion of the stomach is left after the operation of resection. In our experience the surgical correction of benign lesions of the terminal esophagus when performed with a transthoracic approach is not a particularly hazardous undertaking, and we urge strongly that patients not be allowed to become nutritional wrecks before such treatment is recommended.

### SUMMARY

A classification of benign esophageal obstruction due to primary motor insufficiency is described based on physiological, roentgenologic and operative findings.

The clinical findings in 23 patients recently observed are described.

Where feasible, the "U" type of esophagoplasty is recommended as this has given the best results.

When resection is necessary, it is important to resect the acid-secreting portion of the stomach as well as the terminal esophagus in order to prevent postoperative marginal ulceration.

The problem of regurgitation ulceration and excoriation of the esophageal epithelium following operation still remains a considerable one.

7. Womack, N. A.: Esophagoplasty for Esophageal Achalasia, S. Clin. North America **28**: 1241, 1938.

8. Barrett, N. R., and Franklin, R. H.: Concerning the Unfavorable Late Results of Certain Operations Performed in the Treatment of Cardiospasm, Brit. J. Surg. **37**: 194, 1949.

## NEPHROCALCINOSIS

*William J. Engel, M.D., Cleveland*

The term nephrocalcinosis as used in this paper refers to bilateral diffuse calcifications in the renal parenchyma, generally in the pyramids and demonstrable by roentgen examination. In cases of nephrocalcinosis there is disturbed renal function associated usually with hyperchloremia and acidosis. There is also disturbed calcium metabolism; osteomalacia or rickets may eventually develop. Frequently there are few clinical symptoms in the early stages of the disease, but later weakness, anorexia, polyuria and polydipsia may be observed. Sometimes patients with nephrocalcinosis are referred to the urologist because they have passed urinary calculi.

This disorder was described by Butler, Wilson and Farber[1] in 1936. In 1940 Albright and others[2] reported a case of nephrocalcinosis in a 13 year old girl which was associated with rickets and dwarfism. Careful metabolic studies were carried out, resulting in an effective therapeutic regimen. These and two additional cases were described in the monograph of Albright and Reifenstein.[3]

1. Butler, A. M.; Wilson, J. L., and Farber, S.: Dehydration and Acidosis with Calcification at Renal Tubules, J. Pediat. **8**: 489, 1936.

2. Albright, F., and others: Metabolic Studies and Therapy in Case of Nephrocalcinosis with Rickets and Dwarfism, Bull. Johns Hopkins Hosp. **66**:7, 1940.

3. Albright, F., and Reifenstein, E. C., Jr.: Parathyroid Glands and Metabolic Bone Disease, Baltimore, Williams & Wilkins Company, 1948.

From the Cleveland Clinic and the Frank E. Bunts Educational Institute.

Read before the Section on Urology at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 30, 1950.

The early reported cases occurred predominantly in children. Nephrocalcinosis, however, is not confined to children, for Baines, Barclay and Cooke[4] in 1945 reported a case in a woman aged 29 and Greenspan[5] in 1949 recorded a similar case in a man aged 44. In the series of seven cases reported here five are in adults.

Calcification in the renal tubules in children was described by Lightwood[6] (calcium infarction) in 1935, and a series of cases was reported by Anderson[7] in 1939. In none of these, however, was there radiological evidence of the condition, the observations having been made at autopsy.

I have observed three of the seven cases reported here. In presenting the roentgenograms of one of these patients at a recent meeting, three colleagues from widely separated areas of the country came forward to relate similar cases from their practices. In the belief that these cases represent the same condition, they are included in the present report.

## REPORT OF CASES

CASE 1.—An infant boy 4 months of age had nothing significant in his history until a month prior to his admission to the hospital, when he had a febrile illness with temperatures up to 104 F. due to a respiratory infection. At this time he was given sulfadiazine, but an erythematous rash developed while he was taking this medicament, and the mother noted that his urine stained the diapers a brick red. Sulfadiazine therapy was then discontinued, and the patient began to improve.

Two weeks later fever recurred and the administration of sulfadiazine was resumed and continued for seven days. Nevertheless, the condition became worse, and the infant had fever, nausea, vomiting and diarrhea. The mother again noticed the brick dust sediment in the urine, which appeared to be scant. Sulfadiazine was discontinued, and the boy was treated with penicillin. Because of a continued downhill course he was admitted to a hospital in another city where, in spite of further therapy including more sulfadiazine, penicillin and streptomycin, he continued to have an intermittent fever (to 103 F.) and to lose weight. He had oliguria, and urinalysis revealed a trace of albumin. Microscopic examination of the sediment showed epithelial cells, persistent pus cells ranging from 25 to 100 per high power field and occasional red blood cells. His condition did not improve. His fever continued and was attributed to urinary infection. On Oct. 26, 1948 he was referred to the Cleveland Clinic for further investigation.

He was a pale, undernourished and dehydrated infant whose skin was warm and inelastic. The temperature was 101.5 F. General physical examination did not reveal anything significant. The specific gravity of the urine ranged from 1.008 to 1.010. There was a trace of albumin and a persistent pyuria varying from 20 to 40 white blood cells per high power field. A urine culture on Nov. 3, 1948 yielded a growth of Escherichia coli. The blood count showed 3,640,000 red blood cells, hemoglobin 7.8 Gm. and 19,400 white blood cells with 63 per cent lymphocytes. The blood urea was 84 mg. per 100 cc. and the carbon dioxide-combining power 26.2 volumes per cent. The chlorides were 660 mg. per 100 cc., the serum calcium 10.9 mg. and the phosphorus 5 mg. Roentgen examination of the chest revealed no abnormal changes.

Because of the elevated blood urea no immediate cystoscopy or intravenous pyelography was attempted. The diagnosis was thought to rest between a pyelonephritis or an acute toxic nephritis, and the patient was given daily glucose infusions and sodium bicarbonate to combat the acidosis. The blood urea came down to 60 mg. per 100 cc., and on November 9 an intravenous urogram was done. The plain roentgenogram of the abdomen revealed multiple clusters of fine calcifications corresponding with the renal lobules or pyramids. These were so fine as to be scarcely discernible. There was diminished excretion of iodopyracet injection (diodrast®), resulting in poor outline of the renal pelves, but there was sufficient visualization to exclude hydronephrosis or cystic disease of the kidney. Cystoscopy revealed no anomalies or abnormal changes in the bladder. Only one ureteral orifice was present on each side, and each was normal.

The child improved, the temperature returned to normal and the blood urea level came down to 39 mg. per 100 cc. The blood chlorides remained elevated (643 mg. per 100 cc.) but the carbon dioxide-combining power increased to 47.1 volumes per cent. He was eating well and gaining weight, and at the parents' insistence he was discharged from the hospital. At the time of discharge the urine culture had become sterile, but it still showed numerous pus cells. He was placed on a regimen calling for large fluid intake, including milk and vitamin D.

Follow-up roentgenograms in January and in April of 1949 showed an increasing amount of calcification in the renal pyramids. The child was seen again in July 1949. The mother reported he had been feeling well and gaining weight. She had observed that his thirst was excessive and that he might have some fever unless he drank two or three glasses of water the first thing in the morning. There was also polyuria. Physical examination revealed nothing significant. Urinalysis showed a trace of albumin. The specific gravity was 1.010, the $p_H$ 6.0 and there were numerous white blood cells. The blood urea was 57 mg., the chlorides 561 mg., per 100 cc. The carbon dioxide-combining power was 39.0 volumes per cent. A plain roentgenogram of the abdomen revealed a slight increase in the clustered calcifications in the renal pyramids.

Fig. 1 (case 1).—Plain roentgenogram of the kidneys in May 1950. Note pronounced calcifications in renal pyramids.

The child failed to return in spite of an urgent request that the parents bring him in, and I learned they were using some remedy for "kidney stones" suggested by a neighbor. Finally, as the result of a personal visit to the city in which they live, the mother consented to bring the child in for a roentgenogram (May 16, 1950, figure 1). There was a pronounced increase in the renal calcifications. The urine at this visit showed a specific gravity of 1.012, a trace of albumin, many white blood cells and a few red blood cells. The blood

4. Baines, G. H.; Barclay, J. A., and Cooke, W. T.: Nephrocalcinosis Associated with Hyperchloremia and Low Plasma-Bicarbonate, Quart. J. Med. **14**: 113, 1945.

5. Greenspan, E. M.: Hyperchloremic Acidosis and Nephrocalcinosis, Arch. Int. Med. **83**: 271 (March) 1949.

6. Lightwood, R.: Calcium Infarction of Kidneys in Infants, Arch. Dis. Childhood **10**: 205, 1935.

7. Anderson, W. A. D.: Renal Calcification in Infancy and Childhood, J. Pediat. **14**: 375, 1939.

count showed 4,250,000 red blood cells with 10 Gm. (65 per cent) hemoglobin and 12,100 white blood cells. The blood urea was 36 mg. per 100 cc., the plasma chlorides 627 mg. and the carbon dioxide-combining power 43.8 volumes per cent. The child appeared to be well, and there was no bony deformity. Roentgen examination of the bones revealed no evidence of decalcification or rickets. The mother cannot see the need for hospitalizing the child for further study. We have placed him on the regimen of treatment suggested by Albright, and it is hoped that bony changes will be avoided and further renal calcification prevented.

We believe that this baby's problem began with acute toxic nephritis due to sulfonamide intoxication. This was associated with oliguria, hematuria, diminished renal function and a temporary period of nitrogen retention (urea 84 mg. per 100 cc.). As the child improved there was return of normal glomerular function with normal blood urea, but the tubular damage persisted. Hyperchloremic acidosis soon developed. Renal calculi at first were hardly perceptible by roentgen ray, but a series of follow-up films shows a progressive increase in pyramidal calcifications. During this period the patient was not on the regimen of treatment to be described. We believe this case sup-

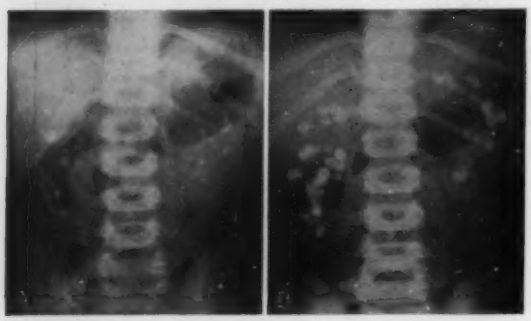

Fig. 2 (case 2).—Plain roentgenogram of kidneys: *A*, April 1949; *B*, May 1950. Note the increase in calcifications and the number of calculi in right renal pelvis. The patient has passed numerous calculi.

plies concrete evidence that the renal calcification is a result of the kidney disease and probably represents the pathological process of calcification in damaged and destroyed renal tubular cells. The evidence furthermore indicates that this damage and destruction was produced by direct toxic action of sulfadiazine. There is no evidence of rickets, and the child's only noteworthy symptoms are polydipsia and polyuria.

CASE 2.—A child aged 2½ years, the brother of the patient described as case 1, did not have any symptoms but was brought in at my suggestion because the mother related that he had been passing small stones. He had first passed stones about two months previously and had since passed several small ones. Except for this he had been well and had developed normally. The mother related that the child had received some type of sulfonamide tablets when he was a small baby because he had a sore throat and fever. She recalls that his diapers were stained at that time, but no particular significance was attached to this observation. The boy was a well developed, husky looking child who was active and apparently well. His general physical examination did not reveal abnormalities.

The urine had a specific gravity of 1.009 and $p_H$ 6.0. There was a trace of albumin, and microscopically there were 10 to 15 white blood cells with numerous clumps and a few red blood cells. The blood count showed 4,860,000 red blood cells, 11.5 Gm. of hemoglobin and 8,600 white blood cells. The blood urea level was 36 mg., sugar 72 mg., serum calcium 11.3 mg. and phosphorus 5.0 mg., per 100 cc. The alkaline phosphatase level was 11.4 Bodansky units. Plasma chlorides and carbon dioxide-combining power were not recorded for this visit.

A plain roentgenogram of the abdomen revealed (fig. 2) extensive bilateral renal calcifications occurring in the renal pyramids, and in addition there were numerous round, opaque shadows lying in the right renal pelvis. An intravenous urogram showed diminished excretion of the contrast medium. The left renal pelvis appeared normal, with the clusters of calcification occurring in the renal pyramids adjacent to the calices. The right renal pelvis was slightly dilated and contained numerous rounded calculi but otherwise presented the same picture as the left. Surgical removal of the stones in the right renal pelvis seemed inadvisable. The parents were instructed to give the boy a large supply of fluids, and vitamin D was prescribed.

The patient was seen again in July 1949. The urine had a specific gravity of 1.012, $p_H$ of 6.0, a trace of albumin and no sugar. Microscopically there were rare red blood cells with four to 12 white blood cells and a few large and small clumps. The blood urea level was 42 mg. and the serum chlorides 577 mg., per 100 cc. The carbon dioxide-combining power was 42.8 volumes per cent and the serum calcium 11.3 mg. per 100 cc.

The boy came in with his brother on May 26, 1950. He had passed several small stones since his last visit. The mother reported that the child had an excessive thirst and passed large amounts of urine; he often experienced enuresis. Urinalysis at this visit showed a specific gravity of 1.012 (early morning specimen) $p_H$ 6.0, albumin (trace) and no sugar. Microscopically there were 15 to 20 white blood cells per high power field. Blood count was 4,800,000 red blood cells, 11.5 Gm. hemoglobin (75 per cent) and 13,800 white blood cells. Blood chemistry studies showed the urea to be 33 mg., creatinine 1.5 mg., sugar 75 mg., and plasma chlorides 610 mg., per 100 cc., and the carbon dioxide-combining power 41.9 volumes per cent. The serum calcium level was 12.5 mg., the phosphorus 5 mg. per 100 cc., and the alkaline phosphatase 10.1 Bodansky units.

Plain roentgenograms of the abdomen revealed extensive nephrocalcinosis with multiple stones in the right renal pelvis. Comparison with roentgenograms made in April 1948 gave the impression that there was some increase in the calcification. Roentgen examination of the right elbow, right wrist and knee revealed no evidence of decalcification or of rickets. The mother could not be persuaded to admit the child to the hospital for further study and treatment. The patient has been placed on Albright's regimen of low salt diet, vitamin D (in the form of Squibb's navitol®) and citrate mixture.

This patient presents the typical picture of nephrocalcinosis which has gone on to the formation of urinary calculi, there being many stones in the right renal pelvis (fig. 2). He has passed a large number of stones. That this is not a familial disease is indicated by the fact that other members of the family are radiologically negative. There is a history of sulfonamide medication during infancy associated with discoloration of the urine consistent with hematuria, crystalluria or both. The boy looks well and is developing normally; there is no radiological evidence of rickets or osteomalacia. He is asymptomatic except that he passes occasional urinary calculi and has polydipsia and polyuria with enuresis.

CASE 3.—A man aged 63 came to the clinic complaining of ulcers of the stomach. No ulcers or other organic disease of the stomach was found. The plain roentgenogram of the abdomen, however, showed multiple bilateral renal calcifications, and the patient was referred to the Urology Department. Further questioning disclosed that four years previously the patient had had a bladder stone removed elsewhere by litholapaxy. Roentgenograms at that time were reported to have shown bilateral renal calcifications. The patient recalled that

some years previous to this time he was treated for "blood poisoning" by the administration of sulfonamide drugs. He could not recall any hematuria or other symptoms of toxicity.

His general physical examination was noncontributory. Urinalysis showed a specific gravity of 1.009 on three different determinations. The $p_H$ was 6.0. There was a trace of albumin but no sugar. Microscopically there were 5 to 8 white blood cells. The Sulkowitch test was reported positive. Right kidney urine and bladder urine cultures were both sterile. The blood urea was 45 mg. per 100 cc. The urea clearance test showed 76 per cent the first hour and 60 per cent the second. Plasma chlorides were 610 mg. per 100 cc., and the carbon dioxide-combining power was 53.2 volumes per cent. Serum calcium and phosphorus were 10.0 and 2.8 mg. per 100 cc., respectively. Serum proteins were 7.0 Gm. per 100 cc. A plain roentgenogram of the abdomen revealed bilateral renal parenchymal calcifications more definite on the left. The intravenous urogram showed adequate excretion of the iodopyracet injection. A retrograde left pyelogram revealed a pelvis anatomically within normal limits, with calcifications in the renal pyramids adjacent to the minor calices.

CASE 4 (Patient of Dr. F. H. Entz, Waterloo, Iowa).—A young married woman had always been perfectly well prior to her second pregnancy, during which she noted malaise followed by a high fever and chills, and a severe pyuria. Roentgenograms taken during this illness were reported negative for any urinary tract calcifications. She was considered to have a pyelitis of pregnancy. With each of the following two pregnancies she had a recurrence of "pyelitis" in the last trimester. She was treated each time with a sulfonamide drug but does not recall that she had any reactions. There had been little trouble between pregnancies, but after the last she had pain in the left flank, pyuria, and intermittent chills with fever.

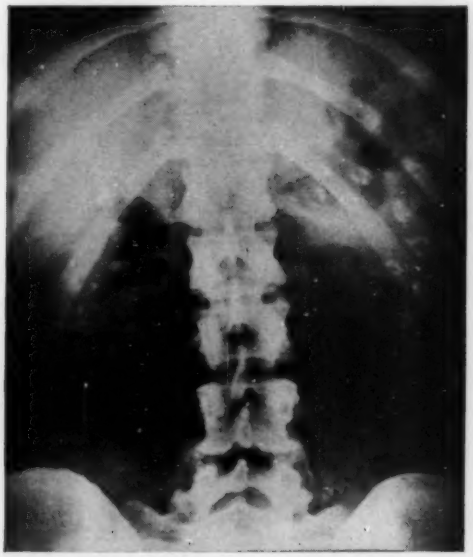

Fig. 3 (case 4).—Plain roentgenogram showing bilateral clustered renal calcifications (patient of Dr. F. H. Entz).

She was admitted to the hospital. The general physical examination revealed essentially normal conditions. The blood pressure was 132/80. The urine contained numerous white blood cells. A plain roentgenogram of the abdomen (fig. 3) revealed definite calcification of both kidneys, the calcifications occurring in clusters corresponding to the renal pyramids. Blood chemistry studies made Feb. 24, 1950 showed chlorides 620 mg. per 100 cc. and carbon dioxide-combining power 60.6 volumes per cent. The serum calcium level was 8.75 mg. and inorganic phosphorus 3.35 mg., per 100 cc. Urinalysis showed a specific gravity of 1.015, no albumin or sugar, many red blood cells and occasional white blood cells.

CASE 5 (Patient of Dr. F. H. Entz, Waterloo, Iowa).—A woman aged 35 entered the hospital complaining of fatigue and anorexia of 36 months' duration. There had been no appreciable loss in weight, but loss of strength had been observed. On admission the diagnosis of Addison's disease was considered. The past history was noncontributory. The

Fig. 4 (case 5).—Plain roentgenogram of the kidneys showing extensive bilateral nephrocalcinosis (patient of Dr. F. H. Entz).

patient had not received any sulfonamide drug to her knowledge, and there was no history of any drug intoxication. The blood pressure was 100/50. There were no abdominal masses or tenderness.

On Feb. 22, 1950 results of blood chemistry studies were: nonprotein nitrogen 53.5 mg., and plasma chlorides 709 mg., per 100 cc.; carbon dioxide-combining power 30.2 volumes per cent; calcium 8.75 mg., and inorganic phosphorus, 4.5 mg., per 100 cc. On March 6, 1950 the plasma chlorides reached 630 mg. per 100 cc.; the carbon dioxide-combining power was 23 volumes per cent. Urinalysis showed a specific gravity of 1.009, a heavy trace of albumin, no sugar and many white blood cells with clumps and numerous epithelial cells. A plain roentgenogram of the abdomen (fig. 4) revealed extensive bilateral renal calcifications.

CASE 6 (Patient of Dr. B. C. Corbus Jr., Fargo, N. D.).—A man aged 45 was referred for investigation of "renal stones." Late in 1943, while he was in military service, he was admitted to a hospital with the complaint of weakness and fatigue. Roentgen examination for suspected arthritis revealed extensive bilateral renal calcifications. Investigations failed to show evidence of hyperparathyroidism. Pyuria was reported, with urine cultures on one occasion growing a Staphylococcus and on another a urea-splitting Micrococcus. The patient was treated with several courses of sulfonamides and mandelic acid. In the latter part of 1948 he passed urinary stones, and subsequently he required repeated care for ureteral and bladder stones. In January 1949 a roentgenogram of the chest revealed evidence of pulmonary tuberculosis. He was placed in a sanatorium where positive sputum smears were reported for tubercle bacilli, but repeated urine examinations were negative. In spite of this, the calcific lesions in the kidney were thought to be due to renal tuberculosis.

Physical examination March 1950 was essentially noncontributory. There was mild kidney tenderness especially in the left costovertebral angle. The blood pressure was 120/80.

The specific gravity of the urine varied from 1.005 to 1.011. There was a trace of albumin, no sugar and 5 to 8 white blood cells per high power field. The Sulkowitch test was positive. Blood count showed 14,800 white blood cells with 75 per cent neutrophils and 16 per cent lymphocytes. The urea nitrogen determination was 10 mg. per 100 cc. Urea clearance was reported as 92 per cent. The serum calcium ranged from 9.8 to 10.2 mg. and inorganic phosphorus from 3.2 to 3.7 mg., per 100 cc. The alkaline phosphatase showed 14, 16 and 17 King and Armstrong units on three determinations. The carbon dioxide-combining power was 48, 56 and 53 volumes per cent. The blood chloride on one examination was reported at 440 mg. per 100 cc.

A roentgenogram of the kidneys (fig. 5) showed extensive bilateral calcifications involving the area of the renal pyramids. Retrograde pyelograms revealed renal pelves of normal size with extensive calcifications distal to the calices. A roentgenogram of the skull showed some demineralization, but otherwise the bone survey was negative. The patient was considered to have chronic pyelonephritis, and treatment was instituted on this basis. His condition remains essentially unchanged.

Fig 5. (case 6).—Intravenous urogram showing extensive bilateral nephrocalcinosis. The portions of the renal pelves visualized with dye appear normal (patient of Dr. B. C. Corbus Jr.).

The radiological picture in this patient appears to be identical with that in the other cases under discussion. The normal urea and urea clearance test indicates satisfactory glomerular function. A single blood chloride determination is within normal limits, and there is little evidence of acidosis in the reported carbon dioxide determinations. It is a little difficult to reconcile this with the other findings, and no ready explanation is apparent. In all other respects this case fits with the group of cases of nephrocalcinosis.

CASE 7 (Patient of Drs. Beck and Vollett, Wilmington, Del.).—A man aged 24 was admitted to the hospital in December 1948 with pain in the left costovertebral angle and left lower abdominal quadrant. The onset had been rather sudden about 24 hours previously, and morphine had been administered. The past history was noncontributory except that in 1945, while the patient was in the Army, he had taken sulfonamide drugs for five months for fever of undetermined origin. He did not recall any hematuria at that time. The physical examination was noncontributory. There was no noteworthy kidney tenderness. The blood pressure was 116/58.

The specific gravity of the urine was 1.012. It gave an acid reaction, albumin 3 plus, no sugar, and was loaded with white blood cells. Bladder and kidney urine cultures all showed no growth of organisms. The blood urea nitrogen level was 14 mg. per 100 cc., the serum calcium 13.0 mg., phosphorus 3.8 mg., and plasma chlorides 445 mg., per 100 cc., and the carbon dioxide-combining power 46 volumes per cent on the only determination available. A plain roentgenogram of the abdomen revealed multiple clustered calcifications in the renal parenchyma corresponding with the renal pyramids. Cystoscopy showed several small calculi in the bladder. The kidney pelves were of normal size with extensive calcifications in the renal papillae adjacent to the calices as shown in bilateral retrograde pyelograms. The roentgenologic findings in this case appear to be identical with those for the group under discussion.

## COMMENT

*Mechanism of Production.*—Albright and his co-workers believed that nephrocalcinosis was of renal origin and was associated with damage to the distal convoluted tubules in the presence of adequate glomerular function. The evidence against this being a glomerular disease is strong. These patients have normal blood urea values, and the urea clearance tests are not significantly altered. The absence of glycosuria, the satisfactory phenolsulfonphthalein excretion and the usually adequate iodopyracet excretion point to intact proximal renal tubular function. Dysfunction of the distal tubules is indicated by the inability of the kidney to concentrate the urine (polyuria and hyposthenuria) and by its failure to secrete an acid urine and by the systemic acidosis. It is believed that the calcification is the result of or follows the renal tubular damage. This theory is supported by data on case 1, which progressed from acute toxic renal injury to calcifications (at first barely perceptible by roentgen ray) to the full blown picture of nephrocalcinosis two years later (fig. 1).

According to Albright [2] the systemic acidosis occurs because in the presence of disease of the distal tubules the kidney is unable to make ammonia and to excrete acids. There is a shortage of base with which to excrete acids, which results in an increased loss of calcium in the urine which acts as a base. It may be presumed that this creates a local metabolic condition favorable for calcification of damaged renal tubular cells. In the case studied by Albright [2] he also postulated that the excessive calcium loss produced a low serum calcium level which induced hyperparathyroidism and a hypophosphatemia resulting in "low phosphorus" rickets. However, rickets is not an essential feature of the condition and would seem merely to be a late manifestation. In neither of the two children in our group of cases is there any evidence of rickets.

There may be other mechanisms involved in the production of acidosis. Pitts and his co-workers [8] postulated a mechanism in the tubule for transportation of acid from the postglomerular blood into the tubular lumen, and it is possible that interference with the enzyme carbonic anhydrase may play a part. Whatever the exact mechanism finally proves to be, it seems clear that the acidosis and hyperchloremia which accompanies this condition is due to disease of the distal tubule. It is also probable that this damage precedes the deposition of calcium.

8. Cited by Greenspan.[5]

*Formation of Calculi.*—Urinary calculi or a history of passing stones was present in five of the seven cases in this series. It seems reasonable to believe that renal tubular calcification is a necessary precursor to stone formation. Calcification may extend down into the collecting tubules and could perhaps eventually project from the renal papilla. Furthermore, small calcific masses may coalesce to form concretions, and there would be a natural tendency for these to be expelled into the renal pelvis. In either event a nucleus for further stone formation would be present and finally the stone would become free to pass into the renal pelvis and down the ureter.

*Cause of Tubular Damage.*—The cause of the tubular damage could not be explained by Albright, although he suggested the possibility of pyelonephritis. In Greenspan's [4] case there was compelling evidence that the original renal damage had been produced by sulfathiazole. Other evidence that the sulfonamides may produce renal tubular damage is furnished by the fact (1) that sulfanilamide inhibits carbonic anhydrase; (2) that Pitts and Alexander were able to produce blood acidosis and urinary alkalosis by administration of sulfanilamide to dogs; (3) that hyperchloremic acidosis had been observed in patients after the use of therapeutic doses of sulfanilamide and hyperchloremic acidosis was reported by Leutscher and Blackman after therapeutic doses of sulfathiazole; (4) that Antopol and associates were able to reproduce chronic calcifying nephrosis confined to the distal tubules after severe transient sulfonamide toxicity in animals, and (5) that in pathological studies by Lucké and French, 153 soldiers were shown to have died with acute toxic lesions due to various sulfonamide drugs. The most characteristic renal lesion was a lower nephron nephrosis involving the distal tubules. In many cases there were calcifications in the distal tubules. In addition to this evidence cited by Greenspan, nephron dissection studies carried out by Oliver [9] showed disruption of the wall of the distal tubules with fragments of epithelium scattered among the invading proliferations of connective tissue.

The sequence of events in case 1 makes it appear highly probable that the renal damage was due to sulfonamide intoxication. The history in this baby's brother (case 2) also permits one to attribute the initial tubular damage to sulfonamide administration. In six of the seven cases there was a definite history of previous sulfonamide medication, although known toxic manifestations were not observed in all cases. It does not seem unreasonable, however, to postulate that tubular damage from a sulfonamide could occur without obvious clinical manifestations. A short siege of hematuria is not infrequently observed in patients who are taking sulfonamides, and the patient may present no subjective symptoms. Transient polyuria and hyposthenuria have also been observed, which would indicate inability of the tubules to concentrate urine.

Thus there is abundant evidence to indicate the role of the sulfonamides in producing direct toxic action on the distal tubules, and I wonder whether it is not more than coincidental that the reporting of these cases, which seem to be occurring with greater frequency, coincides chronologically with the introduction of sulfonamide therapy. There are, of course, other causes for renal tubular damage, and it should not therefore be inferred that all cases of nephrocalcinosis are due to sulfonamide intoxication.

## TREATMENT

The treatment of nephrocalcinosis has been worked out by Albright and his co-workers.[2] Although they were in large measure concerned with the correction of rickets, which was present in the case studied by them, the fundamental principles are the same in nephrocalcinosis with or without rickets. Treatment is designed to (1) relieve the acidosis, (2) reduce the hyperchloremia and (3) correct the negative calcium balance by (*a*) reducing the hypercalciuria and (*b*) improving the calcium absorption.

It was found that the acidosis could be effectively corrected by giving 60 cc. a day of a "citrate mixture" which consists of 140 Gm. of citric acid and 98 Gm. of sodium citrate in 1,000 cc. of water. This supplies added base and creates an intestinal acidosis and a blood alkalosis. With this mixture it has been shown that the carbon dioxide increases and the blood chlorides diminish.

Although reduction of the blood chlorides follows the above measure, it is also advisable to restrict sodium chloride in the diet of these persons. Albright showed that the kidneys are not able to excrete acids, including the chloride radicals; therefore chloride intake should be restricted. It will also be apparent that in the management of these cases saline solution should not be administered when there is need for parenteral fluids.

The hypercalciuria is corrected by supplying added base in the form of "citrate mixture," which relieves the demand for calcium to act as a base. In this disease there is interference with calcium absorption. Browne and Vineberg [10] showed that in acidosis, gastric acidity is decreased. This would tend to decrease calcium absorption from the gastrointestinal tract, thus contributing to the development of osteomalacia. The citric acid in the "citrate mixture" helps to correct this by producing an intestinal acidosis. However, Albright found that the addition of vitamin D further improved calcium absorption: a reduced fecal calcium was observed following its administration. Reduction of calcium loss and improvement in its absorption probably makes unnecessary the administration of calcium, but this should be liberally supplied in the diet in the form of milk and other calcium-containing foods.

Thus these patients should be on a low salt diet, "citrate mixture," vitamin D in normal doses and a diet containing adequate calcium. It is well to recall that excessive vitamin D administration should be avoided to prevent the possible effects of hypervitaminosis on the kidney. On such a regimen Albright noted a diminution in the amount of calcifications in the kidney in addition to dramatic correction of the

9. Oliver, J.: New Directions in Renal Morphology: Method, Its Results and Its Future, Harvey Lectures, 1944-1945, Baltimore, Williams & Wilkins Company, 1945, p. 102.
10. Cited by Albright and Reifenstein.[2]

"rickets" of his patient. The polydipsia in these cases is undoubtedly the result of the inability of the kidneys to concentrate urine, leading to polyuria. This cannot be corrected, therefore these patients must be allowed liberal fluid intake to meet their natural demand.

The treatment of the urinary calculi deserves no special comment since it differs in no way from the usual management of this problem. These calculi are often small enough to pass down the ureter, and it would seem that open surgical intervention for calculi in the renal pelvis should be avoided unless demanded by ureteropelvic obstruction; whenever necessary, operation should be delayed until metabolic balance has been restored by a period of treatment.

## SUMMARY AND CONCLUSIONS

Seven cases of extensive bilateral nephrocalcinosis are presented, two in children and five in adults. All showed characteristic roentgen findings of clusters of calcific deposits in the renal pyramids.

The available laboratory studies are not conclusive in all cases. However, I believe these belong in the groups of cases described in the literature as associated with hyperchloremic acidosis.

Evidence is presented which is in keeping with Albright's conception that this type of nephrocalcinosis is of renal origin and is the result of damage and dysfunction chiefly of the distal convoluted tubules. We believe that the calcification follows and is secondary to the tubular damage.

We believe this tubular damage may in many cases be due to the direct toxic action of sulfonamides. This would seem to be the cause clearly in case 1. In 6 of the 7 cases there was a definite history of antecedent sulfonamide medication.

The disease is not restricted to any age group. Our youngest patient was 4 months of age and the oldest 60 years of age. A wide geographic distribution is also noted.

In cases of this kind the patient is often under the care of the urologist because urinary calculi may form and be passed. It is therefore important that this condition be kept in mind as a cause of urinary calculi.

## ABSTRACT OF DISCUSSION

DR. BEN D. MASSEY, Pasadena, Calif.: The etiologic basis of nephrocalcinosis is obscure and the incidence admittedly rare. Dr. Engel has thoroughly covered the clinical aspects and has stated that the condition is the result of disturbed homeostasis brought about by renal tubular insufficiency and is to be distinguished from renal rickets, in that this condition shows insignificant glomerular damage. Albright has considered ascending pyelonephritis involving the tubules as a possibility. However, infection was demonstrated in only two of the eight cases he reported. In the original case reported by Butler, Wilson and Farber in 1936, no urinary cultures are mentioned. The evidence presented by Dr. Engel is strongly suggestive that the sulfonamides can be an etiological factor. The relatively infrequent incidence of nephrocalcinosis in patients receiving sulfonamide therapy suggests a localized tubular sensitivity to the drug rather than a specific poison, and this may occur without gross clinical signs. In support of sulfonamide as an etiological factor Baines, Barclay and Cooke reported in 1945 the case of a woman aged 29 who had bilateral renal stones, elevated serum chloride, decreased plasma bicarbonate level and a relatively fixed urinary specific gravity and $p_H$. This patient responded to the sodium citrate and citric acid therapy but died after a severe reaction to sulfathiazole. In other words, there did exist a possible sensitivity to the drug. The implication of this paper ties in with the clinical observation that many patients receiving sulfonamide therapy have a persistent acidosis in spite of the administration of alkalies, and this will continue until the sulfonamide therapy is discontinued. The acidosis is an evidence of tubular toxicity and should be regarded as an immediate indication to discontinue the drug.

DR. ROGER W. BARNES, M.D., Los Angeles: Dr. Engel has brought to our attention a rare and little understood pathological entity. His assumption that the ingestion of sulfonamides might be a factor in producing this condition is interesting. It is evident that one cause is metabolic disturbance, but it may well be true that some other factor such as the ingestion of some toxic substance is a factor. In the only similar case which we have seen the patient had a severe dermatitis due to chronic arsenic poisoning. It was discovered that the patient's husband had been putting ant paste into her coffee for several months in an effort to make it easy for him to get a new wife. This patient had not been taking sulfonamides; her calcium and phosphate determinations and her basal metabolic rate were normal.

DR. W. J. ENGEL, Cleveland: It is true that at present nephrocalcinosis must be regarded as a rare disease, but I am inclined to believe that the incidence may be increasing. I do not consider all cases of nephrocalcinosis to be the result of sulfonamide intoxication, but it is interesting to note that the reporting of such cases coincides chronologically with the introduction and greater use of the sulfonamide drugs. There are doubtless other causes of distal tubular damage which could be followed by calcification. Thinking with regard to kidney disease probably should be revised. We have been accustomed to considering the kidney as an organ. Actually it is only an accumulation of nephrons which are the important functional units. Dr. Gene Oliver has emphasized the importance of considering disease of the nephron, and here we have an example of a disease apparently involving a selected portion of the nephron, i. e., the distal convoluted tubule. As urologists we are especially interested because it appears that we have here a mechanism for the production of some urinary calculi. One may even wonder whether the calcified plaques on the renal papillae described by Randall might be formed in this manner. Thus the calcification might form in the distal tubule, work its way down the renal pyramid and cling to the renal papilla until it drops off as a calculus.

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**New Bone.**—Calcium metabolism and bone physiology may well be viewed together since more than 99 per cent of the total calcium content of the body resides in the bones and teeth. The skeleton is a living and not an inert tissue. New bone is constantly being formed and bone is ever being resorbed, not necessarily at the same rates in all bones or even in any one area of a given bone. This has long been known to the pathologist who sees deposition of new bone along one side of a trabecula and its removal on the other side. Since so small a percentage of calcium resides outside the bones, it should be a simple matter to determine whether more bone is being laid down than is being resorbed by observing the calcium balance—i. e., if more calcium is going into the body than is coming out, then bone mass must be increasing and vice versa. In general this is true, but such an overall balance will not disclose where the new bone is being laid down, and one part of the skeleton might be very active in osteogenesis, another very active in osteolysis, and the sum of the two would equalize. Furthermore, balance experiments are difficult to carry out, and caution must be observed in the interpretation of short-term experiments, for considerable quantities of both calcium and phosphorus (up to several grams) may lie in the gut, presumably in an inert state; especially is this precaution necessary after large changes in the calcium content of the diet or when peristalsis suddenly slows to a point of cessation of stools as in total intravenous feeding.—John Eager Howard, Metabolism of Calcium and Phosphorus in Bone, *Bulletin of the New York Academy of Medicine*, January 1951.

# TREATMENT OF PATIENTS WITH CARCINOMA OF THE BLADDER

*R. H. Flocks, M.D., Iowa City*

Because of improvements in the technics of ureterointestinal anastomosis, cystectomy and partial cystectomy, there is need for a reevaluation of the indications and contraindications of the various types of treatment for patients with carcinoma of the bladder. A review of 540 patients with carcinoma of the bladder treated at the University Hospital from the years 1932 to 1942, a study of more recent patients treated more radically and a review of the recent literature emphasize the need for individual treatment of these patients.

In order to adequately evaluate the various types of therapy, a basis of reference for classifying these tumors is necessary. This has been generally recognized. Jewett and Strong [1] have shown that the microscopic anatomic structure or grade of malignancy of an infiltrating carcinoma of the bladder reveals only the potentiality of the tumor for rapid growth and

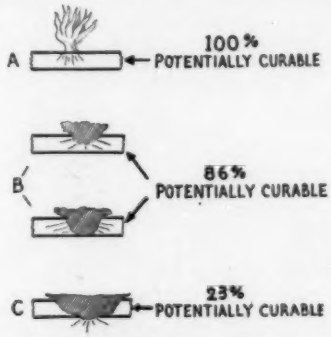


Fig. 1.—Diagram illustrating Jewett's classification of bladder tumors based on depth of penetration of the tumor into the bladder wall.

metastasis but does not, in itself, indicate the presence or absence of metastasis or extravesical extension and therefore does not indicate whether thorough local destruction or removal of the tumor will produce a cure. On the contrary, they have shown that the depth of penetration of the tumor into the bladder wall is a more reliable indication of spread beyond the bladder wall and therefore urge classification on this basis (fig. 1). Their classification has been made use of by many investigators (Shackman,[2] Jewett, Flocks [3] and others), and table 1 indicates the classification of our series on this basis. However, a study of the failures in our series shows that this classification, although serviceable in itself, is not enough to evaluate the efficacy of a particular surgical procedure in destroying potentially destroyable tumors. The location of the tumor in the bladder, the multiplicity of the tumors, the involvement of lymph nodes, the invasion of the prostate and infection and obstruction in the upper urinary tract are also extremely important considerations. A combination of studies—cystography, pyelography, cystoscopy, bimanual palpation, biopsy and at times even surgical exploration—is necessary to obtain this information.

Table 2 indicates the types of therapy used at present for the treatment of carcinoma of the bladder. These are essentially loop resection and electrocoagulation either transurethrally or through the open bladder, partial cystectomy, total cystectomy, lymph node removal and the various forms of irradiation. What is the place of these forms of therapy in the treatment of carcinoma of the bladder?

TABLE 1.—*Results of Treatment in Carcinoma of the Bladder in 540 Patients*

| Type of Tumor | Group* | Total Series | % of Total | Controlled | | Number Not Followed | Number Known Dead or Dying with Disease |
|---|---|---|---|---|---|---|---|
| | | | | No. | % | | |
| Papillary carcinoma..... | A | 168 | 31.1 | 130 | 77.4 | 3 | 35 |
| Infiltrating within bladder wall | B | 249 | 46.1 | 99 | 39.7 | 35 | 114 |
| Infiltrating through bladder wall ..... | C | 123 | 22.8 | 2 | 1.6 | .. | 121 |
| | | 540 | | 231 | 42.8 | 38 | 270 |

* Jewett's classification.

Before I attempt to answer the question just presented, I must emphasize the place of ureterointestinal anastomosis in the treatment of patients with carcinoma of the bladder. This operation is playing a greater and greater role in their management. The two great causes of failure in the management of patients with carcinoma of the bladder are inadequate destruction of the neoplasm and upper urinary tract damage due to obstruction and infection. Ureterointestinal anastomosis prior to the application of treatment to the neoplasm permits more nearly complete surgical treatment, electroresection and coagulation and more intensive application of the various forms of irradiation. It permits the adequate control of upper urinary tract obstruction and infection, and it should be used

TABLE 2.—*Surgical Treatment of Carcinoma of the Bladder*

1. Destruction of the tumor by electrocoagulation
   - (*a*) Transurethrally
   - (*b*) Through a suprapubic cystotomy
2. Removal of the tumor by surgical procedures
   - (*a*) Partial cystectomy
   - (*b*) Total cystectomy and prostatoseminal vesiculectomy and lymphadenectomy
     - With ureterointestinal anastomosis
     - With cutaneous ureterostomy
3. Diversion of the urine followed by destruction of the tumor by electrocoagulation or irradiation, or both
4. Palliative treatment
   - (*a*) Ureteral transplantation
     - Into bowel
     - To skin
   - (*b*) Suprapubic cystostomy
   - (*c*) Transurethral electrocoagulation

unhesitatingly when the ureters are an obstacle to satisfactory destruction of a neoplasm. Also, as will be indicated later in the course of this paper, ureterointestinal anastomosis is of great help in the palliative treatment of inoperable lesions. Moreover, occasionally

From the Department of Urology, State University of Iowa.

Read before the Section on Urology at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 30, 1950.

1. Jewett, H. J., and Strong, G. H.: J. Urol. 55: 366, 1946.
2. Shackman, R.: Brit. J. Surg. 35: 140, 1947.
3. Flocks, R. H.: Canad. M. A. J. 55: 348, 1946.

the diversion of the urinary stream from the bladder with the consequent decrease in bladder irritation and diversion of possible carcinogens from the urinary tract seems to have a specifically beneficial effect on the neoplasm. Neoplasms known to exist prior to the

Fig. 2.—Drawing of the actual appearance of an area at the bladder neck during coagulation with the high frequency current applied through the resectoscope. Note the white lines where the heat has concentrated along vascular and lymphatic channels.

performance of this procedure have disappeared after diversion of the urinary stream from the bladder.[4]

Transurethral resection with electrocoagulation of the base of the tumor was the form of treatment most commonly used in our series of patients for the destruction of the neoplasm (tables 3 and 4). This proved to be an efficient method of destroying the tumor. In approximately 50 per cent of those patients with lesions proved histologically to have fallen in group B (Jewett), good results were obtained by transurethral resection. In 77 per cent of those patients with minimal infiltration, good results were obtained by transurethral

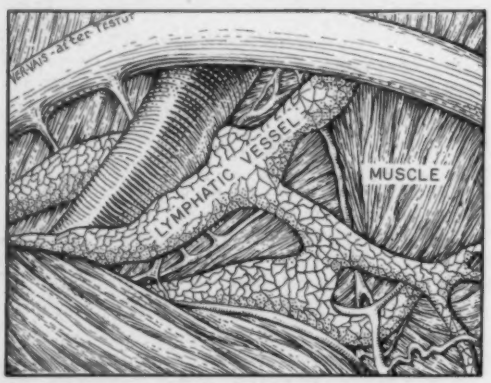


Fig. 3.—Drawing after Testut of the intramural lymphatic channels. Note their relationship to muscle and the blood vessels.

resection (table 5). These results contrasted with a potential curability of 86 and 100 per cent, respectively. The advantages of this method of destroying the tumor are these: The results are relatively good. They are obtained without manipulation and thus avoid the danger of squeezing tumor cells into lymphatic vessels. The method causes the spread of heat in the lymphatics and vessels for some distance beyond the limits of coagulation, thus destroying tumor cells which may already be in transit to form a metastasis (figs. 2, 3, 4 and 5). It does all this without the danger of spillage of cells outside the bladder and thus outside of reach. Moreover, this technic is associated with a low mortality and morbidity and no change in bladder function.

A study of the failures showed that certain situations predisposed to a poor result. When the tumor was located near the bladder neck anteriorly or in the fundus it was difficult to reach and destroy easily with the resectoscope; a large percentage of the tumors in

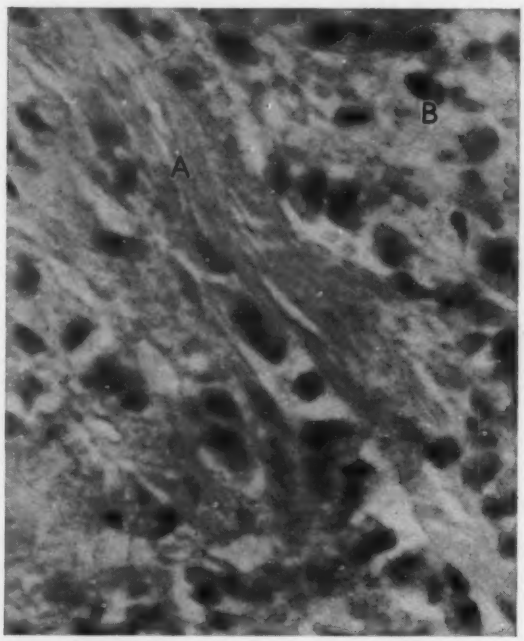


Fig. 4.—Microscopic appearance of tissue deep in the bladder wall before transurethral coagulation: *A*, muscle bundle; *B*, tumor.

these locations were thus inadequately destroyed. Moreover, in no case in which the prostate was involved, unless this involvement was minimal and superficial, was the tumor controlled by this technic. Multiple tumors were controlled less easily, even though they were group A of Jewett, and were the main cause of failure to control the tumors in group A patients. In 28 per cent of the cases one or more of the above factors plus possible lymph node involvement was the cause of failure to control the tumor. In 13 per cent of cases infection, which now could be adequately controlled with the antibiotics plus diversion of the urinary stream, was the primary cause of a poor result. Therefore, it would seem that, given a few tumors, the correct location, the absence of lymph node involvement, adequate control of infection, and avoidance of fear of cutting through the bladder wall,

4. Davis, E.: Disappearance of Carcinomatous Ulceration of Bladder Following Ureterosigmoidostomy: Report of 2 Cases, J. A. M. A. **137**: 450 (May 29) 1948. Goldberg, L. G.: J. Urol. **63**: 116, 1950.

intensive transurethral resection and coagulation is the method of choice for destroying the tumor in group A and group B patients (figs. 6, 7 and 8).

Cautery through the open bladder has some advantages and some disadvantages over the closed method. It may make possible more nearly adequate electrocoagulation in certain locations, such as at the bladder neck anteriorly or laterally. It avoids the extensive manipulation associated with partial cystectomy in those locations, but it may be associated with spillage. It allows for examination of the lymph nodes and possibly their removal down to the bladder. It is of no value

TABLE 3.—*Results of Treatment of 168 Papillary Tumors, Group A (Jewett)*

| Treatment | No. Treated | Operative Deaths | No. Controlled | No. Not Followed | No. Dead or Dying of Disease |
|---|---|---|---|---|---|
| Transurethral resection... | 167 | 11 | 130 | 3 | 23 |
| Suprapubic fulguration... | 1 | 1 | ... | .. | .. |

TABLE 4.—*Results of Treatment of 249 Patients with Infiltrating Carcinoma Confined Within the Urinary Bladder, Group B (Jewett)*

| Treatment | No. Treated | Operative Deaths | No. Controlled | No. Not Followed | No. Dead or Dying of Disease |
|---|---|---|---|---|---|
| Transurethral resection..... | 126 | 6 | 67 | 16 | 36 |
| Transurethral resection plus roentgen therapy..... | 74 | .. | 23 | 18 | 33 |
| Partial cystectomy..... | 13 | 2 | 5 | .. | 6 |
| Suprapubic fulguration..... | 16 | 5 | 1 | 2 | 8 |
| Roentgen therapy alone..... | 6 | .. | .. | .. | 6 |
| Radon seeds..... | 1 | .. | .. | .. | 1 |
| Radium suprapubically..... | 1 | .. | 1 | .. | .. |
| Total cystectomy..... | 2 | .. | 2 | .. | .. |
| Ureterointestinal anastomosis | 2 | .. | .. | .. | 2 |
| Bilateral pyelostomy..... | 1 | 1 | .. | .. | .. |
| No treatment..... | 7 | .. | .. | .. | 7 |

TABLE 5.—*Analysis of Group A Treatment*

Group A (Jewett) — 100% potentially curable
167 cases treated by transurethral coagulation..... — 77% controlled

Cause of difficulty:
(*a*) Multiple tumors with extensive coagulation → infection of upper urinary tract → death
(*b*) Change in character of tumors → death due to malignancy

Correction:
Divert urine and do total cystectomy

in multiple tumors because these are difficult to see and the possibility of contamination and local spread is high. All in all, its possibilities are limited.

The place of partial cystectomy in the treatment of infiltrating carcinoma of the bladder has recently been described by Jewett and Cason.[5] In certain locations (anteriorly at the bladder neck, even with some involvement of the prostate, or at the fundus) it is the procedure of choice. Here, in locations reached with difficulty with the resectoscope, the tumor and even its associated lymphatics may be widely removed with little manipulation and with little danger of spillage. On the contrary, when the trigone is involved or the posterior portion of the bladder neck is extensively involved, wide excision without too much manipulation is usually impossible and total cystectomy becomes the procedure of choice. In our series 13 partial cystectomies were performed in group B patients with a 40 per cent five year survival. Again the poor results

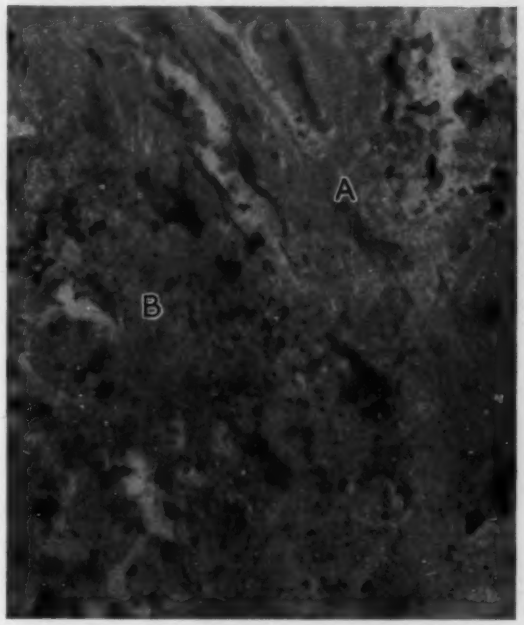


Fig. 5.—Same as figure 4, one month after transurethral coagulation. Note that muscle bundles (*A*) with their nuclei are relatively unharmed while tumor (*B*), which was apparently spreading along lymphatic channels, is necrotic.

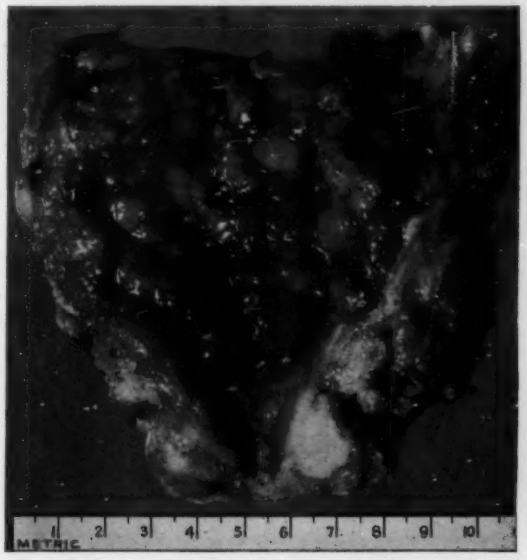


Fig. 6.—Bladder of a patient with a tremendous number of group A tumors. Good result after total cystectomy.

were associated with inadequate removal of the tumor because its location was not suitable for treatment by partial cystectomy (figs. 9, 10 and 11).

5. Jewett, H. J., and Cason, J. F.: South. M. J. 41: 158, 1948.

Total cystectomy with transplantation of the ureters is now a relatively safe procedure. Immediate mortality ranges from 5 to 12 per cent and with growing experience is much nearer the lower figure than the higher. Marshall and Whitmore [6] had only a 31 per cent two year survival with simple cystectomy for

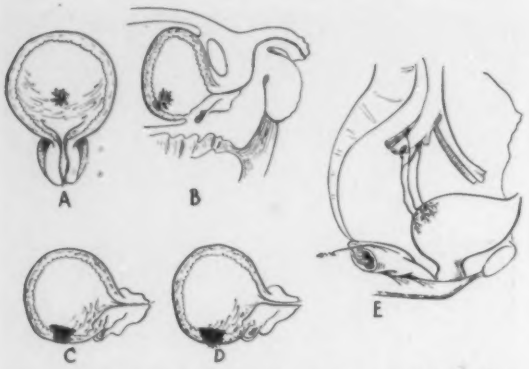


Fig. 7.—Diagrams illustrating position of tumor most favorable for transurethral treatment. Even when the condition illustrated in *D* exists, extensive coagulation plus removal of lymphatics may be satisfactory although most such cases would be found to be inoperable. *A* and *B* show a group A tumor; *C* shows a group B tumor.

infiltrating carcinoma limited to the bladder wall. It is probable that the two important factors accounting for this low survival rate are manipulation and lack of removal of the lymphatics (figs. 12 and 13).

The extent to which manipulation of the tumor, with consequent squeezing of tumor cells into the lymphatics or blood vessels which are not removed, plays a part in the local recurrence and distant metastasis after partial and total cystectomy is difficult to gage. These happenings are not uncommon after operative procedures, but whether their seeds were present before operation or whether the manipulation incident to the

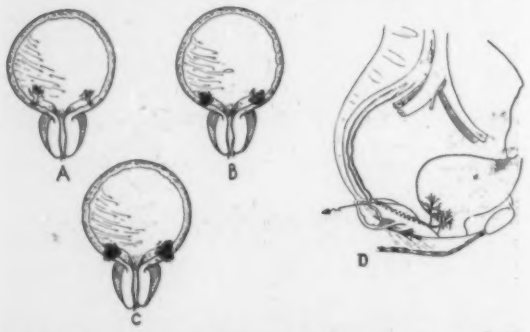


Fig. 8.—Diagrams illustrating another location suitable for transurethral treatment. The condition in *C* may necessitate total cystectomy.

procedure was the cause cannot be easily proved. The work of Batson [7] illustrating the extensive venous anastomosis about the bladder neck should be recalled with regard to this problem. The posibility of spread by this means should always be considered, and that operative procedure should be carried out which is associated with the least manipulation of the tumor. It is our belief that preoperative roentgen therapy might be of great value in lessening the dangers of this complication.

Leadbetter and Cooper [8] in a classic report emphasized the place of regional gland dissection for carcinoma of the bladder. They emphasized from such postmortem studies as those of Spooner,[9] Colston and Leadbetter [10] and Jewett, that approximately 50 per cent of group B and C patients have metastasis

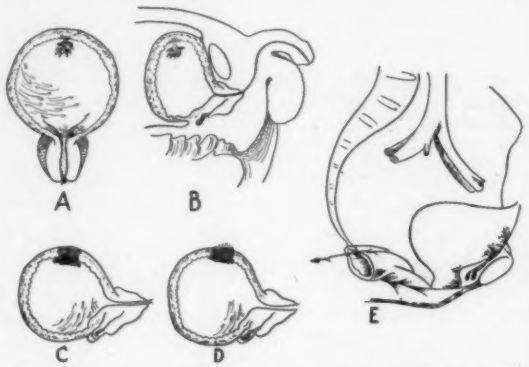


Fig. 9.—Diagrams illustrating a position which can be treated by transurethral methods but is relatively unfavorable. This is in an ideal location for partial cystectomy with removal of regional lymphatics.

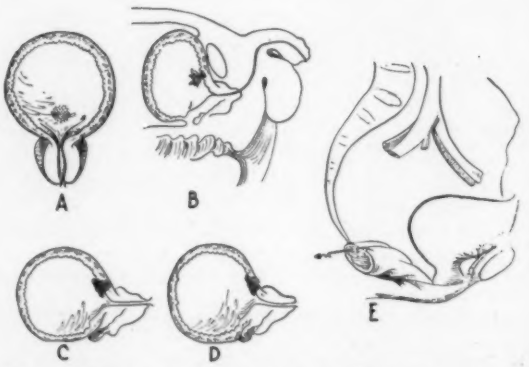


Fig. 10.—Diagram illustrating location exceedingly unfavorable for transurethral treatment because it is extremely difficult to get the resectoscope in position to adequately destroy the tumor. Partial or total cystectomy is indicated here.

and approximately 15 to 25 per cent of this group had only lymph node involvement. There was an equal percentage of patients who had distant metastasis without regional lymph node involvement. In these metastases the routes of spread were probably the blood vessels. In cases of deeply infiltrating carcinoma of the bladder, removal of the pelvic lymphatics may be expected to extend the limits of palliative and curative treatment. Leadbetter and Cooper reviewed the work on the anatomy of the vesical lymphatics. A system of lymphatic channels starts in the wall of the

6. Marshall, V. F., and Whitmore, W. F.: J. Urol. **63**: 232, 1950.
7. Batson, O. V.: Ann. Surg. **112**: 138, 1940.
8. Leadbetter, W. F., and Cooper, J. F.: J. Urol. **63**: 242, 1950.
9. Spooner, A. D.: Tr. Am. A. Genito-Urin. Surgeons **27**: 86, 1934.
10. Colston, J. A. C., and Leadbetter, W. F.: J. Urol. **36**: 669, 1936.

bladder, extending through intercalated lymph nodes, particularly on the lateral aspect of the bladder and in the prevesical space to the external iliac nodes, the internal iliac nodes, the sacral nodes and the obturator nodes and the common iliac nodes. It is possible by dissection to remove in partial cystectomy the regional nodes and the adjacent lymphatics as illustrated in figures 6 to 12, inclusive, and to do this even more radically in those situations where total cystectomy is performed. The sacral lymphatics are usually not removed in this procedure but may be readily removed by pelvic viscerectomy.[11] The above facts must be considered in the management of the patient with infiltrating carcinoma of the bladder.

Irradiation was used in 82 of the group B patients and 30 of the group C patients (table 6). There was some evidence of improvement as the result of this therapy, but on the whole it seemed to be of little value as a sole means for destruction of the tumor. This has not, however, been the experience of others, such as Montgomery,[12] Barringer[13] and Milner.[14] A study of our experience shows that the limitations are

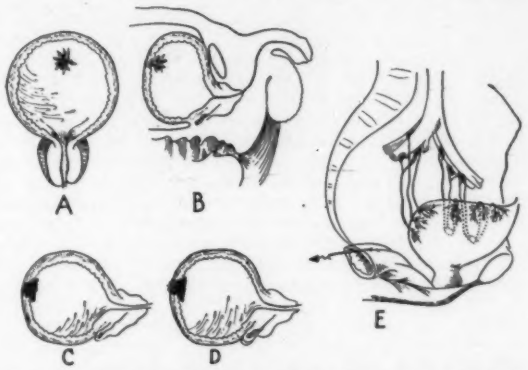


Fig. 11.—Diagram illustrating a position which is also exceedingly unsuitable for transurethral treatment. The resectoscope cannot be placed in such a position to resect the tumor adequately and safely. The position is ideal for partial cystectomy with removal of the regional lymphatics.

similar in essence but in some respects greater than those of transurethral resection and electrocoagulation. They are due to the presence of the tumors in such locations that adequately destructive irradiation cannot be applied to all portions of the neoplasm. In selected cases, such as multiple papillomatosis, intravesical application of radium as described by Lloyd Lewis[15] may be of value. It is my belief also that preoperative roentgen treatment to close off small vessels and lymphatics might greatly lessen the dangers due to manipulation of the tumor at the time of partial and total cystectomy. A program of combined therapy for selected cases: preoperative high voltage roentgen therapy followed by partial or total cystectomy plus removal of the pelvic lymphatics has been initiated at the University Hospitals.

Palliative treatment plays an important part in the care of patients with carcinoma of the bladder. One hundred and twenty-three of our 540 patients (23 per cent) had inoperable lesions. Many of these had great discomfort due to bladder irritation or hemorrhage from the tumor. The procedures of choice for relief of these discomforts are transurethral resection to control bleeding and enlarge the bladder capacity and ureterointestinal anastomosis to divert the urinary stream from the bladder. The latter procedure is assuming greater and greater importance as the method of choice for palliation (tables 7 and 8).

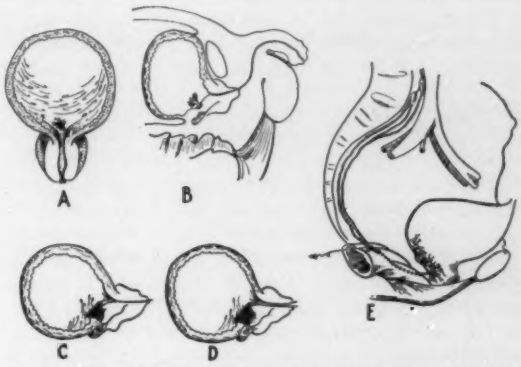


Fig. 12.—Diagram showing tumor involving the prostate. Unless the involvement is superficial as illustrated in *A* and *B*, where transurethral resection is adequate, total cystectomy with removal of the prostate, seminal vesicles and regional lymphatics is usually indicated.

## SUMMARY

A review of the treatment of 540 patients with carcinoma of the bladder with special emphasis on the failures reveals the need for individualizing the treatment for each patient. This individualization will

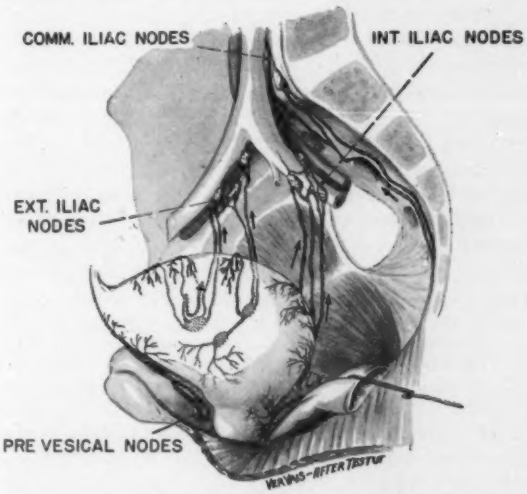


Fig. 13.—Diagram after Testut illustrating the regional lymphatics of the bladder. The sacral lymphatic vessels with the common iliac and sacral nodes are usually not easily accessible unless viscerectomy is performed.

depend on the age and general condition of the patient, the location of the tumor, the grade of the tumor, the depth of the bladder wall involvement, the multiplicity

11. Brintnall, E. G., and Flocks, R. H., to be published.
12. Montgomery, T. R.: Personal communication to the author.
13. Barringer, B. S., in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, 1943, Vol. VIII, Chapter 16.
14. Milner, W. H.: Personal communication to the author.
15. Lewis, L. G.: Radium in Bladder Cancer, Urologists' Letter Club, Aug. 1, 1949.

of the tumors, the presence or absence of regional lymph nodes or distant metastasis, and the condition of the upper part of the urinary tract.

Transurethral resection and electrocoagulation are best used for lesions limited to the bladder and not located anteriorly at the bladder neck, in the fundus or deeply invading the prostate.

Partial cystectomy is best used for lesions on the anterior wall of the bladder, even if the prostate is involved, and for lesions in the fundus of the bladder.

TABLE 6.—*Analysis of Group B Treatment Results*

| | |
|---|---|
| Group B (Jewett)<br>249 cases | 86% potentially curable<br>39% controlled |
| 126 treated transurethrally | 54% controlled |
| 74 treated transurethrally plus irradiation | 31% controlled |
| 13 treated by partial cystectomy | 40% controlled |
| 33 treated by miscellaneous methods | 10% controlled |
| **Difficulties:** | |
| 1. Primarily infection, local or ascending | 13% (34 cases) |
| 2. Primarily lack of destruction of tumors | 28% (66 cases) |
| 3. Mortality | 6% (14 cases) |
| 4. Unfollowed | 14% (36 cases) |
| **Correction:** | |
| 1. Divert urine and more adequately destroy the tumor | |
| 2. Partial cystectomy and lymphadenectomy in selected cases | |
| 3. Total cystectomy and lymphadenectomy in selected cases | |
| 4. Irradiation as an adjunct | |

TABLE 7.—*Analysis of Group C Treatment Results*

| | |
|---|---|
| Group C (Jewett)<br>123 cases | 23% potentially curable<br>2% controlled |
| 12% (14 cases) died primarily of infection | |
| 53 treated by transurethral resection with temporary improvement in 69% (35 cases) | |
| Ureterointestinal anastomosis in 7 cases produced excellent palliation. This raises question of its more frequent use plus extensive coagulation or irradiation, or both, in selected cases to raise percentage of controlled cases. | |

TABLE 8.—*Deeply Infiltrating Carcinoma of the Bladder*

| | |
|---|---|
| Total no. of cases: 372 | No. controlled: 101 (27%) |
| Potentially (Jewett) this group should have had 242 (65%) cases controlled | |
| Urinary tract infection accounted for | 48 cases (13%) |
| Mortality accounted for | 22 cases ( 6%) |
| Unfollowed cases accounted for | 44 cases (12%) |
| Carcinoma itself accounted for | 157 cases (42%) |

The value of diversion of the urinary stream for the prevention and treatment of upper urinary tract obstruction and infection must be emphasized. Ureterointestinal anastomosis, moreover, will permit more extensive surgical and irradiation therapy for destruction of the tumor.

In more extensive lesions and in multiple papillomatosis total cystectomy with lymphatic removal and irradiation must be considered. The possible dangers of manipulation of the tumor and the possible value of preliminary high voltage roentgen treatment for its avoidance are discussed.

The value of transurethral electrocoagulation and ureterointestinal anastomosis as palliative treatment is emphasized.

## ABSTRACT OF DISCUSSION

DR. BEN D. MASSEY, Pasadena, Calif.: I am more confused today than I was five or ten years ago about what is the satisfactory treatment. Certainly for the multiple tumors of the bladder—and I am speaking of grade 2 carcinoma—the open attack is preferable to the transurethral method, both as to the ability to cover all areas involved and the depth and the extent of the coagulation. Associates and I have experienced difficulty in choosing the proper method for those needing more radical treatment, namely, cystectomy or segmental resection of grade 3 carcinoma on an area which lends itself to wide resection. A wide excision of the bladder and removal of a deep segment of pericystic tissue in some instances seems to offer an equal chance of cure with less disability than a poor cystectomy. Yet we have observed recurrences at the ureteral orifice after wide removal of the bladder for a small grade 3 lesion at the junction of the dome and lateral wall. I believe that the lymphatic drainage on the lateral wall goes toward the ureteral orifice of that side, and with that in mind on one occasion we did a hemicystectomy, taking off the bladder to the midline, implanting one ureter into the bowel and closing up the bladder. The patient has been well for several years, and there is no evidence of recurrence. In infiltrating lesions or grade 3 papillary lesions near the trigone, bladder neck or in the posterior urethra we do a bloc removal of the prostate, seminal vesicles and bladder and transplantation of ureters to the bowel.

DR. ROGER W. BARNES, Los Angeles: Dr. Flocks has classified the treatment of patients with carcinoma of the bladder in such a manner as to give definite indications for the different modes of treatment. Jewett's classification, based on the amount of infiltration of the tumor into the bladder wall, is helpful in determining the amount of extravesical extension both by direct invasion and by metastases. However, it is important to consider also the grade of malignancy based on the histological structure when one is making a decision as to the best mode of treatment in a given case. As Dr. Flocks has pointed out, the manipulation of a tumor during cystectomy is a factor in producing postoperative metastases and extension. The more malignant tumors are more easily spread by manipulation. After total cystectomy for grade 3 and 4 tumors there is often a rapid recurrence of neoplastic tissue in the prevesical space and early signs of more distant metastases. This fact has led some urologic surgeons to avoid cystectomy in patients who have these more malignant tumors. Transurethral resection avoids the manipulation and when it is done thoroughly on the smaller tumors, or when palliation such as diversion of the urinary stream is carried out on the more extensive growths, the morbidity and mortality are less than following cystectomy. Grade 2 neoplasms and some of the papillomatous or grade 1 tumors which are extensive and which recur rapidly after their removal from the bladder, should be treated by cystectomy, for there is much less danger of spreading these tumors by manipulation. Dr. Flocks' suggestion of using preoperative roentgen therapy is pertinent and might prevent recurrence in the more highly malignant neoplasms. Dr. Flocks used in only one case a mode of treatment that I believe is useful in helping to prevent recurrence of the tumor after transurethral resection. I refer to the use of radon emanation seeds implanted into the tumor-bearing area of the bladder wall. This treatment is indicated in tumors of more than grade 1 malignancy which are suitable for transurethral or suprapubic resection. Four years ago at the California State meeting, we reported a series of cases which showed the advantage of the use of radon seeds. In a comparative study of 122 cases in which this treatment was used with another series of 227 similar cases in which resection only was done, there was a significant difference in favor of those who had the radon implanted.

DR. G. J. THOMPSON, Rochester, Minn.: I had hoped that Dr. Flocks would establish definite indications for various types of treatment. A clue on how one might properly treat a tumor can be gained from careful survey of the excretory cystogram. Combined with cystoscopic findings such evidence sometimes justifies comparatively conservative transurethral

treatment rather than total cystectomy. When the bladder wall is distensible and the tumor confined to an easily reached area, one would hesitate to advise total cystectomy. Transurethral procedures will effect a cure in a high percentage of these cases. When the bladder is small and undistensible, the border of the tumor is poorly defined and biopsy shows a high grade lesion, probably no method of treatment will be successful. Palliative roentgen therapy or, if the history is not too long, surgical exploration with a view to total cystectomy sometimes succeeds but more often fails because of extravesical extension of the growth. We have treated patients having high grade neoplasm both transurethrally and by cystectomy. The five year survival rates are better in those treated by transurethral resection. However, it must be admitted that many of the patients who were selected for transurethral resection had smaller lesions, even though of a high grade of malignancy. But in some who had extensive tumor and treatment, when combined with high voltage roentgen therapy, did prove effective. When transurethral operation is the method selected, we find that tumors in the lower half of the bladder in the region of the trigone and on the lower part of the lateral walls and on the anterior wall near the vesical neck are best treated with the Thompson resectoscope. A tumor on the posterior wall or high on the anterior wall can be excised most easily with the loop type of resectoscope. In removing a tumor high in the dome it is important to have an assistant push the bladder wall down into a position where it can be reached. It is sometimes necessary to remove a portion of the prostate gland in order more adequately to reach a growth. Fulguration of the underlying muscle, after adequate removal of the tumor, is, of course, important. We employ postoperative roentgen irradiation when the border of the tumor is poorly defined. If it is a small lesion with cleancut edges, radon seed implantation seems preferable.

DR. RUBIN H. FLOCKS, Iowa City: Dr. Thompson's comments are pertinent, and I agree with them wholeheartedly. Our results with transurethral resection in these cases, compared with the results that Dr. Victor Marshall published on total cystectomy for similar cases, apparently show that transurethral resection is superior to total cystectomy as it is done at the present time for that type of case. From study of our poorer results the location of the tumor seemed to be important. Whether it was a question of being unable to cut deeply, especially in those areas at the bladder neck and anteriorally, I do not know, but the incidence of recurrence and later death—recurrence that could not be controlled—in comparison to the results in tumors of similar grade which occurred anteriorly was definitely much higher than in those which could easily be reached by the resectoscope. We are now more likely to do open surgery when there is extensive invasion of the prostate or when the lesion occurs directly in front in the fundus or anteriorly close to the bladder neck, where it is not easily reached by the resectoscope.

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**Food Sensitivity to Cereals.**—There is . . . agreement among physicians who have made a particular study of the role of food allergy by means of adequate diagnostic procedures that the commonly ingested cereal grains are the most common food allergens. Rowe, who pioneered our clinical interest in food allergy, has emphasized for many years the importance of basic diagnostic diets eliminating the major cereal grains and, in his most recent works lays greatest stress on a single cereal-free elimination diet which also omits eggs and milk as well as a group of several other foods. Rinkel's experience as well as our own indicates that corn and wheat sensitivity are the two most important causes of chronic food allergy, there being no statistically significant difference between the incidence of sensitivity to these two cereal grains. There is also general agreement that multiple cereal sensitivity is either very common or is likely to be readily induced in an individual already specifically sensitized to one or more members of the cereal grain botanical family.—Theron G. Randolph, M.D., Concepts of Food Allergy Important in Specific Diagnosis, *The Journal of Allergy*, November 1950.

# Q FEVER STUDIES IN SOUTHERN CALIFORNIA

## SUMMARY OF CURRENT RESULTS AND A DISCUSSION OF POSSIBLE CONTROL MEASURES

*Robert J. Huebner, M.D.*
*and*
*Joseph A. Bell, M.D., Bethesda, Md.*

For the past two and a half years representatives of the United States Public Health Service, the California State Department of Public Health and health departments of the county and city of Los Angeles, assisted by many local physicians, have been investigating the occurrence of Q fever in Southern California. These studies began in 1947 following Young's discovery of Q fever among patients in Artesia,[1] a dairy community located in Los Angeles County. Shepard and Huebner found that 15 of 17 patients with Q fever in this area lived close to dairies or visited them and that serums of many local dairy cows contained antibodies for the disease.[2] Huebner, Jellison and others recovered Coxiella burnetii, the causative agent of Q fever, from the milk of cows and showed that the pooled raw milk of two thirds of 63 dairies tested in the Los Angeles area contained the organism in large quantities.[3] These and other workers have carried out extensive epizootiological studies of C. burnetii infection in cattle and other possible sources of human infection in the Los Angeles area. Beck, Bell and other workers[4] conducted epidemiological studies of 300 cases and developed hypotheses as to the source of human infection. Bell, Beck and associates have tested these hypotheses by numerous epidemiological studies of some 10,000 residents of the area. The results of many of these studies have been published,[5] but additional and more detailed reports will be forthcoming. We propose here to summarize the results of the epizootiological and epidemiological studies and to discuss their influence on possible control measures. It should be pointed out that the Q fever problem as it exists in the Los Angeles area is not necessarily representative of some of the other areas in which Q fever is known to occur.

### EPIZOOTIOLOGICAL STUDIES

Epizootiologic studies have been conducted in the endemic area for more than two years by a team of field investigators including entomologists and veterinarians. The direction of these investigations was

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From the Microbiological Institute, National Institutes of Health, Public Health Service, Federal Security Agency.

Read in a Symposium on Q Fever before the Section on Preventive and Industrial Medicine and Public Health at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 30, 1950.

1. Young, F. W.: Q Fever in Artesia, California, California Med. **69**: 89-90, 1948.

2. Shepard, C. C., and Huebner, R. J.: Q Fever in Los Angeles County: Description of Some of Its Epidemiological Features, Am. J. Pub. Health **38**: 781-788, 1948.

3. Huebner, R. J.; Jellison, W. L.; Beck, M. D.; Parker, R. R., and Shepard, C. C.: Q Fever Studies in Southern California: I. Recovery of Rickettsia Burneti from Raw Milk, Pub. Health Rep. **63**: 214-222, 1948.

4. Beck, M. D.; Bell, J. A.; Shaw, E. W., and Huebner, R. J.: Q Fever Studies in Southern California: II. An Epidemiological Study of 300 Cases, Pub. Health Rep. **64**: 41-56, 1949.

5. Bell, J. A.; Beck, M. D., and Huebner, R. J.: Epidemiologic Studies of Q Fever in Southern California, J. A. M. A. **142**: 868-872 (March 25) 1950.

determined by epidemiological findings; therefore they were largely focused on Los Angeles dairy herds and dairy environs. However, these studies were extended, whenever indicated, to other areas and to other animal species. Intensive studies were conducted to determine the prevalence and manifestations of infection among dairy cattle as well as to obtain information concerning methods of spread. Considerable data have been accumulated; some have been published [6]; some remain to be analyzed.[6b] Some of the more important observations which have a bearing on the chief purpose of this report are listed below.

In addition to demonstrating C. burnetii in the pooled milk of a majority of 63 dairies tested, the following results were obtained:

1. Surveys demonstrated serum antibodies against Q fever in cows of 30 widely scattered dairies in Los Angeles and suggested that more than 10 per cent of all cows in the area were constantly infected.[7] As in tests of human serums,[5] a standardized, comparatively insensitive complement fixation technic was used. When evaluated in terms of demonstrable infection in the milk of cows [7] this test was found to be a highly specific indication of the presence or absence of concurrent infections with C. burnetii.

2. Clinical illness attributable to Q fever infection was not apparent among naturally infected dairy cattle, and infection appeared to have little or no effect on milk production.

3. Observations which were continued for 20 months among several of the large dairy herds revealed a tendency for the prevalence of infection to increase in most of them.[7] Chart 1 shows the rates obtained in one herd at various intervals during 21 months. Except for one dairy, where the prevalence dropped slightly over the same period, the curve shown in chart 1 appeared to be representative of most similar herds. Studies of individual cows showed that many of them retained infection throughout the entire period of observation.

4. Two separate studies of the prevalence of infection among uninfected cows imported into three representative dairies in two different years (1948 and 1949) showed that some became infected within several weeks, many in two to three months and more than 40 per cent within six months after arrival.[7] No appreciable differences in prevalence were noted in the three herds included in the two studies.

5. Infection among Los Angeles dairy bulls appeared to be almost nonexistent, as indicated by tests of serum in the complement fixation test.[7]

6. Preliminary studies of pasteurization procedures and of commercially pasteurized milk indicated that viable C. burnetti were greatly reduced in number but were not completely eliminated from all pasteurized milk specimens.[6a] Laboratory studies of the resistence of C. burnetii to heat showed that temperatures in excess of 145 F. were required to inactivate all organisms when suspended in milk placed in sealed vials and submerged in water baths for 30 to 40 minutes.[8]

7. Parturient placentas of infected cows were shown to contain as many as 100,000,000 infectious doses for guinea pigs [6e] per gram of tissue. Since infection and parturition are frequent occurrences among Los Angeles dairy cows, it is obvious that tremendous numbers of organisms are deposited from this source on the hides of calves and on the ground of open corrals where, in the warm, dry climate, desiccation quickly occurs. Contamination of calves and the environment is also produced by raw milk of infected cows. However, the infectiousness of raw milk for guinea pigs has not been shown to exceed 10,000 infectious doses per milliliter, and usually only 100 to 1,000 such doses can be demonstrated.[7]

8. The tissues of Otobius megnini, the spinose ear tick taken from dairy cows, were shown to contain C. burnetii.[6b] This tick is not known to attack man, and its possible role in the spread of Q fever among cattle is undetermined.

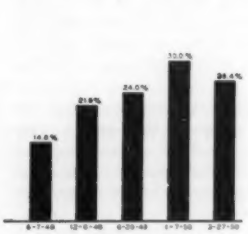


Chart 1.

Chart 1.—Infection among milk cows of a representative Los Angeles dairy herd (400 to 500 cows) as indicated by the percentage of positive complement fixation tests of serums taken at specified intervals.

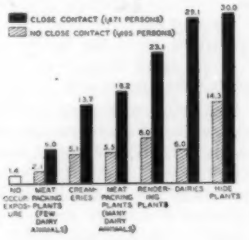


Chart 2.

Chart 2.—Effect of occupation: Percentage of employees with positive complement fixation according to intensity of exposure to cattle and their products.

Numerous other arthropods were tested from time to time and all were negative except for one pool of ticks (Dermacentor occidentalis) collected in scrub lands outside the dairy area.

9. Pilot studies of the prophylactic value of a vaccine (killed C. burnetii) that was administered to uninfected cows at the time of their introduction into each of three herds showed that subsequent infections among the vaccinated cows of each herd were less than one third as frequent as among comparable controls.[9]

10. Sheep and goats [10] were investigated whenever epidemiological studies of cases indicated that association with these species occurred. A strain of Q fever was isolated from the lacteal secretions of several sheep. Repeated attempts, at various intervals between 1947 and 1949, to demonstrate C. burnetii in the pooled milk of goat dairies in the Los Angeles area resulted in one equivocal isolation of the organism.

## EPIDEMIOLOGICAL STUDIES

Clinical manifestations resembled those observed in previous studies. The illnesses were most commonly characterized by high fever, malaise, weakness, headache, a pneumonitis demonstrable by roentgenogram and considerable variation in severity and duration. Mild, moderately severe and serious illnesses occurred

6. (*a*) Huebner, R. J.; Jellison, W. L.; Beck, M. D., and Wilcox, P. F.: Q Fever Studies in Southern California: III. Effects of Pasteurization on Survival of C. Burnetii in Naturally Infected Milk, Pub. Health Rep. **64**: 499-511, 1949. (*b*) Jellison, W. L.; Bell, E. J.; Huebner, R. J.; Parker, R. R., and Welsh, H. H.: Q Fever Studies in Southern California: IV. Occurrence of Coxiella Burnetii in the Spinose Ear Tick (Otobius Megnini), ibid. **63**: 1483-1489, 1948. (*c*) Jellison, W. L.; Ormsbee, R.; Beck, M. D.; Huebner, R. J.; Parker, R. R., and Bell, E. J.: Q Fever Studies in Southern California: V. Natural Infection in a Dairy Cow, ibid. **63**: 1611-1618, 1948. (*d*) Jellison, W. L.; Welsh, H. H.; Elson, B. E., and Huebner, R. J.: Q Fever Studies in Southern California: XI. Recovery of Coxiella Burnetii from the Milk of Sheep, ibid. **65**: 395-399, 1950. (*e*) Luoto, L., and Huebner, R. J.: Q Fever Studies in Southern California: IX. Isolation of Q Fever Organisms from Parturient Placentas of Naturally Infected Dairy Cows, ibid. **65**: 541-544, 1950. (*f*) Huebner, Jellison, Beck, Parker and Shepard.[3]

7. Huebner, R. J.; Jellison, W. L.; Luoto, L., and Winn, J.: Unpublished data.

8. Ransom, S., and Huebner, R. J.: Thermal and Chemical Resistance of Coxiella Burnetii, read before the Annual Meeting, Society of American Bacteriologists, Baltimore, May 14-18, 1950, to be published.

9. Luoto, L.; Winn, J. F., and Huebner, R. J.: Q Fever Studies in Southern California: Vaccination of Dairy Cattle Against Q Fever, to be published.

10. Caminopetros, J.: Q Fever (Balkan Grippe), in Proceedings of the Fourth International Congresses on Tropical Medicine and Malaria, Washington, D. C., May 10-18, 1948, Department of State Publication 3246, Washington, D. C., Government Printing Office, 1949, pp. 33-34. Lennette, E. H.; Clark, W. H., and Dean, B. H.: Sheep and Goats in the Epidemiology of Q Fever in Northern California, Am. J. Trop. Med. **29**: 527-541, 1949.

simultaneously in several small outbreaks, each presumably having a common source of infection. A separate report [11] of 80 hospitalized cases presents a detailed account of the more severe illnesses. Three deaths due to Q fever were encountered in 1948 during the case study period.

An epidemiological study of 300 cases showed that males from 20 to 59 years of age were predominantly infected, but cases also occurred in many females and in persons of other ages, ranging from 3 to 75 years. Cases occurred during all seasons of the year. Forty-five per cent of the patients lived within ¼ mile of a dairy, 38 per cent had occupation in livestock industries and 32 per cent used raw milk in their households. The percentage of infections associated with these three attributes was disproportionately high as compared to the incidence in the general population, but it was fully realized that these cases did not necessarily reflect the natural occurrence of the disease in the area. Furthermore, infection was believed to be much more widespread than indicated by the illnesses which were brought to the attention of the investigators.[12] Thus a study limited to cases would only permit hypothesis as to the chief source of human infection.

In order to obtain more definite information about the natural sources of human disease in Los Angeles, numerous specific epidemiological studies were undertaken in selected population groups of that area. These studies were designed to identify the chief sources of human infection in the area and to show whether persons most apt to be infected were those who lived near dairies, who worked with livestock or who used raw milk in their households.

*Validity of the Survey Methods.*—It was immediately obvious that an interpretation of the epidemiological studies in Los Angeles would depend on the accuracy and the meaning of the particular laboratory serological test used for demonstrating previous infection. A comparatively insensitive complement fixation test was selected for these studies. This test had been used satisfactorily for more than seven years in studies of Q fever and other rickettsial diseases at the National Institutes of Health. However, in order to obtain more specific information an evaluation of the Q fever complement fixation test was conducted prior to and during the Los Angeles studies. Complement fixation tests were performed on human serums collected during the course of hundreds of infections known to be Q fever and also on serums collected from more than 2,000 persons selected as controls from various groups living and working in areas other than California. Some of these control specimens were obtained during surveys of population groups having occupational exposure to livestock, and many represented specimens from persons with illnesses other than Q fever. This study, which will be given in more detail in another communication,[12a] provided evidence that the test was consistently reproducible and highly specific in that tests of noninfected persons were 99.7 per cent negative.

*Results of Epidemiological Surveys.*—The specific epidemiological studies embraced nearly 10,000 persons in industrial and residential groups preselected to represent certain degrees of contact with livestock and their raw products, particularly milk.[8] Epidemiological histories and blood samples for complement fixation tests were obtained on each person. The accompanying table shows the proportions of positive reactions obtained among 12 different population groups. The highest rates of positive reactions occurred in persons having the most intimate contact with dairy cows, their raw products and other livestock; the lowest rates were observed among groups having little or no contact with such materials. Since available evidence indicates that the positive reactions represented Q fever infections occurring within the recent past, and since positive reactions did not correlate with any of the many other attributes studied (such as associations with other animals), these observations support the belief that dairy cows represent the most important sources of human infection with Q fever in the Los Angeles area.

*Percentage of Persons Positive to Complement Fixation Test in Various Population Groups in Los Angeles*

| Population Groups | Percentage Positive |
|---|---|
| Dairies | 23.0 |
| Fat rendering plants | 21.6 |
| Hide and wool plants | 16.1 |
| Homes using raw milk | 12.9 |
| Meat packing plants (many dairy animals) | 11.4 |
| Creameries | 8.1 |
| Fertilizer plant | 7.9 |
| Residential group in dairy area | 6.9 |
| Meat packing plants (few dairy animals) | 3.9 |
| Aircraft manufacturing | 1.4 |
| Residential group (non dairy area) | 1.3 |
| Routine premarital serum | 1.2 |

*Residence Near Dairies.*—The earliest and one of the most persistent epidemiological observations to be made during the Q fever study was that an extremely high proportion of patients lived near dairies which were later found to contain infected cows.[13] This high proportion of cases appeared to have been partially influenced by several small outbreaks that occurred among persons living in households adjacent to dairy corrals.[14] During a six month period in 1947 there were 17 cases observed among persons living in an auto trailer community adjacent to a large dairy known to contain over 150 infected cows. During this period approximately 10 cases also occurred among employees of this dairy. It was interesting that none of the 17 patients in the trailer camp community used milk from the nearby dairy or worked with livestock. Additional evidence concerning the possible influence of residence near dairies on positive reactions was obtained in five

11. Denlinger, R. B.: Clinical Aspects of Q Fever in Southern California: A Study of 80 Hospitalized Cases, Ann. Int. Med. 30:510-527, 1949.

12. Huebner, R. J.; Jellison, W. L., and Beck, M. D.: Q Fever: A Review of Current Knowledge, Ann. Int. Med. 30: 495-509, 1949.

12a. Huebner, R. J.; Beeman, E. A., and Turner, H.: Unpublished data.

13. Shepard and Huebner.[2] Beck, Bell, Shaw and Huebner.[4] Bell, Beck and Huebner.[5]

14. Huebner, R. J.; Beck, M. D., and Bell, J. A.: Unpublished data.

specific surveys, including approximately 1,000 persons living within ¾ mile of infected dairies of various sizes; 6.9 per cent were positive for Q fever, which far exceeded the 1.3 per cent with positive reactions in the general population groups. Persons having residence nearest a dairy tended to have a higher proportion of positive reactions than those living farther away from the dairy.

*Occupational Exposure to Livestock.*—Practically all natural epidemics of Q fever have occurred among persons having occupational or military activities involving livestock, their products or environment. Thus infected livestock appears to be the source of most human infection and only rarely is the human patient or a tick bite the source of human disease.[15] In Southern California the case studies and the various population group studies confirmed these observations in an endemic area.[4]

Specific studies of serum antibodies among seven separate occupational groups showed that persons employed in livestock and dairy industries had a higher proportion of positive reactions than those who were not so employed (table). In addition, persons working within various livestock industries who had intense contact with livestock or their raw products consistently showed higher proportions of positive reactions than those who had less intense contact (chart 2).

*Raw Milk as a Source of Human Infection.*—Early epidemiological studies of cases of Q fever in Los Angeles were compatible with those described in other areas where cattle were implicated as sources of infection (Australia,[15d] Texas,[15b] Switzerland [16]). Except for unrelated sporadic cases in persons using raw milk, but not otherwise exposed to known reservoirs of infection, there was little evidence at first to suggest that raw milk was an important source of infection. However, when C. burnetii was found in the pooled raw milk of the majority of 60 dairies in the area,[5] and when 32 per cent of 300 patients [4] were found to have used raw milk in their households, the whole matter had to be reviewed in a different light. Consequently, a specific study was undertaken among the users of raw milk, living in households several miles from the dairy area. This study was carefully controlled by concomitant investigations of four times as many persons living in adjacent households, almost all of whom did not use raw milk. The survey included almost 2,000 persons, and the results are summarized in chart 3. It was quite clearly shown that regular and recent use of raw milk greatly influenced the prevalence of serologic evidence of prior infection.

Additional data concerning the influence of raw milk on human infection were obtained in studies among 895 persons living in four residential areas in the Los Angeles milkshed (chart 4). These studies once again suggested that household use of raw milk influenced the prevalence of positive reactions.

Considerably more information on this point was also obtained in seven large-scale studies of occupational groups, including more than 50 separate plants and a total of 5,702 persons. Analysis again showed that in every study persons who used raw milk had a higher proportion of positive reactions than those who did not use raw milk. The results obtained in five of these occupational groups are shown in chart 4.

As a further comment on the association between the use of raw milk and Q fever infection, the results obtained in studies of creamery workers were particularly interesting. First of all, during the case study

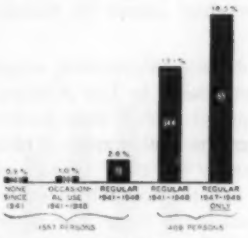

Chart 3.

Chart 3.—Effect of raw milk: Percentage of persons with positive complement fixation according to period and regularity of use of raw milk in Los Angeles (1948).

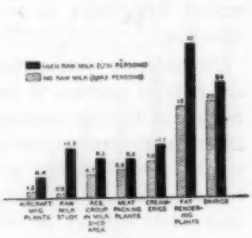

Chart 4.

Chart 4.—Percentage of persons with positive complement fixation in various population groups in Los Angeles according to the use of raw milk.

illnesses due to Q fever were observed in a number of creamery workers. In the occupational group studies practically none of the 730 creamery workers had exposure to livestock, but these workers were constantly exposed to large amounts of infected milk. It was interesting that evidence of infection in this group exceeded by seven times that of the general population—an observation which remained significant when adjusted for the personal use of raw milk in their households. Furthermore, persons with intense occupational contact with raw milk in the creamery accounted for almost three times as many positive reactions as did persons with less intense contact (chart 2). These observations constitute additional evidence that raw milk can produce Q fever infections; it also suggests that the ingestion of raw milk is not necessary to account for such infections.

Thus, each of many independent studies of occupational and residential groups, embracing a total of almost 10,000 persons, gave evidence that raw milk was responsible for a considerable proportion of human infections with C. burnetii in the Los Angeles area.

15. (*a*) Derrick, E. H., and Burnet, F. M.: Q Fever, in Proceedings of the Sixth Congress of the Pacific Science Association, Berkeley, Calif., University of California Press, 1940, vol. 5, pp. 745-752. Robbins, F. C.; Gauld, R. L., and Warner, F. B.: Q Fever in the Mediterranean Area: Report of Its Occurrence in Allied Troops; II. Epidemiology, Am. J. Hyg. **44**: 23-50, 1946. (*b*) Topping, N. H.; Shepard, C. C., and Irons, J. V.: Q Fever in the United States: I. Epidemiologic Studies of an Outbreak Among Stock Handlers and Slaughterhouse Workers, J. A. M. A. **133**: 815-818 (March 22) 1947. (*c*) Smith, D. J. W., and Derrick, E. H.: Studies in the Epidemiology of Q Fever: I. The Isolation of 6 Strains of Rickettsia Burneti from the Tick Haemaphysalis Humerosa, Australian J. Exper. Biol. & M. Sc. **18**: 1-8, 1940. Davis, G. E., and Cox, H. R.: A Filter-Passing Infectious Agent Isolated from Ticks: I. Isolation from Dermacentor Andersoni, Reactions in Animals, and Filtration Experiments, Pub. Health Rep. **53**: 2259-2267, 1938. Derrick, E. H.: "Q" Fever: A New Entity; Clinical Features, Diagnosis and Laboratory Investigation, M. J. Australia **2**: 281-299, 1937. (*d*) Derrick, E. H.; Smith, D. J. W., and Brown, H. E.: Studies in the Epidemiology of Q Fever: The Role of a Cow in the Transmission of Human Infection, Australian J. Exper. Biol. & M. Sc. **20**: 105-110, 1942.

16. Gsell, G.: Rickettsia Burneti Pneumonias: The "Q" Fever of Switzerland, Méd. et hyg. **5**: 317, 1947.

*Illness Among Persons with Positive Serologic Reactions.*—The positive serologic reactions were associated with clinical illness in these studies. Illness records obtained prior to bleeding on more than 6,000 persons showed that 48 per cent of those with positive reactions had given a history of prior febrile illness suggestive of Q fever, whereas only 27 per cent of those with negative reactions gave such a history. This ratio, which was observed consistently in the various studies, including the specific raw milk study, provides good evidence that the excess of illness among the positive reactors was due to previously unrecognized Q fever.

## COMMENT ON CONTROL IN SOUTHERN CALIFORNIA

C. burnetii occurs chiefly as an infectious parasite of a variety of animals. Infection of man is not necessary for the propagation and survival of the parasite in nature. All evidence indicates that man is an incidental host and that infection of man results almost exclusively from contact with infected animals, their products or their environments. In the Los Angeles area dairy cattle have been the sources of human infection for at least several years. It seems likely that Q fever will continue to be a public health problem in this area until specific measures can be devised for its control.

Control of infection in man may be approached by erecting effective barriers to spread of infection between animals and humans, by increasing the resistance of humans, e. g., by vaccination, or by control of infection in animal reservoirs.

Universal pasteurization represents one available method which can be expected to reduce the number of cases resulting from the use of milk. Despite the demonstration of small amounts of viable C. burnetii in a few commercially pasteurized milk specimens,[6a] pasteurization has been shown in the foregoing studies to effectively reduce the occurrence of infection. Furthermore, there is no good evidence that pasteurized milk is an important source of human infection. Vaccination of laboratory personnel intensely exposed to infection shows much promise [17] and presumably may eventually prove to be of value in protecting special groups naturally exposed to rich sources of infection. However, universal pastuerization and vaccination of intensely exposed persons can be expected only to reduce the total number of cases, since in the Los Angeles area the existence of multiple avenues of dissemination of infection implies a need for different types of barriers, some of which are impractical or simply unavailable.

Control of infection from animal sources appears to be the most promising method for control of the human disease. Unfortunately, studies of the well established and extensive infection which exists among dairy herds in California provide no evidence that this will be accomplished through the operation of natural forces. Present evidence indicates that the prevalence of infection among herds in that area is increasing and suggests that the spread to animals in noninfected areas is a distinct possibility. There is evidence that C. burnetii infection does not produce obvious or easily observable pathological conditions in cattle and may not influence milk production in dairy cows. This is fortunate for our milk supply and for the dairy industry, but it removes some of the economic incentives that exist, e. g., in brucellosis, for dairy men to study methods for control of animal infection. Information concerning methods of spread among cattle and other animals is meager and provides no basis for specific attempts at this time to prevent spread of C. burnetii among them. The promise shown by experimental vaccination of dairy cows requires that long term and more extensive studies be carried out to determine its effectiveness as a practical method of control.

At the present time, therefore, wholly effective means for control of Q fever in Southern California are not at hand. It is desirable that the public be informed of the problem, that milk be pasteurized, that the disease be reportable in endemic areas, that laboratories be available and used to study the continued prevalence of infection in animals as well as in man and that studies be carried out to develop practical and effective methods of control.

## SUMMARY AND CONCLUSIONS

The discovery of Q fever in the Los Angeles area of California in 1947 provided an opportunity for studies of sources and modes of spread of the disease in an endemic area. Epidemiological study of 300 cases and numerous epidemiological studies of almost 10,000 persons in selected population groups provided considerable evidence, in addition to that already available in previous studies of Q fever, that the major factor in the spread of Q fever to man is association with infected livestock. In more detail these studies clearly showed that dairy cattle and some of their raw products were the most frequent sources of human infection in the Los Angeles area. Persons most apt to become infected are those who have occupational exposure to livestock, those who live near a dairy or livestock yards and those who use raw milk in their households.

Epizootiological and environmental studies showed that dairy cows and their raw products represented a tremendous reservoir of C. burnetii in the Los Angeles area. The fact that Los Angeles County is a major livestock center and contains one of the largest and most concentrated dairy industries in the world makes it probable that Q fever will remain a public health problem in that area until effective control measures are developed. Although universal pasteurization of milk will help prevent some infections and the vaccination of occupationally exposed groups may afford protection to those groups, it appears that truly effective control of the disease in man must await the development of measures for control of infection in the animal sources of human disease.

17. Snyder, M. J.; Smadel, J. E., and Robbins, F. C.: Vaccination Against Q Fever, J. Bact. 54: 77-78, 1947. Parker, R. R.: Personal communication to the authors. Lennette, E. H.: Personal communication to the authors. Huebner, R. J.: Unpublished data.

# OBSERVATIONS ON THE EPIDEMIOLOGY OF Q FEVER IN NORTHERN CALIFORNIA

*Edwin H. Lennette, M.D.*
*and*
*William H. Clark, M.D., Berkeley, Calif.*

Q fever was described as a new clinical entity by Derrick [1] in 1937. The original description was based on febrile illnesses observed among abattoir workers in Queensland, Australia,[2] and for some years the disease was recognized only in that area. Since 1944, however, the disease has been identified in Mediterranean Europe and Africa, in France, Germany, Switzerland, Rumania and England; in the Western Hemisphere, Q fever has been reported from Panama and several parts of the United States. Prior to 1946 the only authenticated instance of naturally acquired Q fever in the United States was that reported by Hesdorffer and Duffalo [3] in 1941. In 1946 there occurred two large outbreaks of Q fever among workers in meat-packing houses; one outbreak, involving 55 persons, occurred in Amarillo, Texas,[4] the other, involving 33 persons, occurred in Chicago.[5] In May 1947, Q fever was identified in California in the Los Angeles area.[6] Epidemiological studies by Shepard and Huebner [7] and Huebner and others [8] indicated that the disease was endemic in the area and that it occurred among persons who had some contact with dairy cattle. The latter workers also found that the causal organism, Coxiella burnetii, was shed in the milk of infected dairy animals in the area where the human disease was occurring.[8] Since that time Huebner and his associates have conducted intensive studies on the disease in Southern California. This paper deals with some of the observations on Q fever in Northern California.

## SOURCES OF INFECTION

The first cases of Q fever in Northern California were uncovered through the medium of a serologic survey conducted on serum specimens submitted for Brucella agglutination tests. Field epidemiological investigations of these early cases pointed to the probable involvement of domestic livestock other than cattle. In the first instance investigated, the patient, who had been hospitalized for several weeks with an undiagnosed illness, proved to be the owner of a large herd of dairy goats and cows. Serologic examination of the livestock showed that only one of 26 cows possessed demonstrable complement-fixing antibodies to C. burnetii, whereas 12 of 30 goats (40 per cent) were positive. Investigation of the ranch from which these goats had been purchased revealed that 136 of 262 goats (52 per cent) had complement-fixing antibodies. Epidemiological investigation of a second early case revealed that the patient was a sheep rancher and also the owner of a small herd of dairy cows. Complement fixation tests on the blood of the 46 cattle showed that two animals (4.6 per cent) had antibodies; 54 of 96 sheep tested (56 per cent) had antibodies.

As additional cases of Q fever were found in Northern California, it was observed that the majority of them occurred in sheep-raising areas. In one such area 88 cases occurred during 1948 and 1949; in most instances the disease occurred among adult males who had had contact, either by virtue of occupation or residence, with domestic livestock. Only a few of these livestock were cattle, and only a small percentage of these had antibodies. In addition, attempts to recover the Rickettsia from the milk of dairy cows in this area were negative. Sheep was the species to which the majority of the patients had been exposed, and of a sample of 437 sheep representing this livestock contact over 30 per cent were found to possess antibodies. Moreover, the Rickettsia was found to be shed in the milk of sheep.[9]

In this same region, there was an outbreak involving nearly 70 persons in an agricultural college. Contact with livestock was not as obvious in all these cases as in those above, but a significantly large proportion of the cases occurred among students whose major curriculum was animal husbandry. All types of domestic livestock were present as part of the herds used for teaching purposes. When these livestock were examined serologically, it was found that a high proportion (46 per cent) of the sheep had antibodies to C. burnetii. Only three animals of the 184 in the dairy herd, and three of the four goats present, possessed antibodies. Antibodies were not detected in horses or swine.

Epidemiological observations of the foregoing type led to serologic studies on 2,600 sheep in two categories: those animals associated with patients having Q fever and those representing the general sheep population of Northern California. Among those sheep epidemiologically associated in some manner with human cases, nearly 30 per cent were found to possess antibodies; by contrast, only 3.6 per cent of the animals drawn from the general sheep population had antibodies. These observations suggest a relationship between the occurrence of infection in sheep and man but do not necessarily imply causal relationship. The

From the Viral and Rickettsial Disease Laboratory and the Acute Communicable Disease Service, State of California Department of Public Health.

Read in a Symposium on Q Fever before the Section on Preventive and Industrial Medicine and Public Health at the Ninety-Ninth Annual Session of the American Medical Association, San Francisco, June 30, 1950.

1. Derrick, E. H.: "Q" Fever, A New Fever Entity: Clinical Features, Diagnosis, and Laboratory Investigation, M. J. Australia **2**: 281 (Aug. 21) 1937.

2. Q fever is still referred to in the literature as Queensland fever; according to a personal communication from Dr. E. H. Derrick, the "Q" stands for "query," in reference to the many unanswered problems posed by this new disease at the time of his original publication.

3. Hesdorffer, M. B., and Duffalo, F. A.: American "Q" Fever: Report of Probable Case, J. A. M. A. **116**: 1901 (April 26) 1941.

4. Topping, N. H.; Shepard, C. C., and Irons, J. V.: Q Fever in United States: I. Epidemiologic Studies of Outbreak Among Stock Handlers and Slaughterhouse Workers, J. A. M. A. **133**: 813 (March 22) 1947.

5. Shepard, C. C.: An Outbreak of Q Fever in a Chicago Packing House, Am. J. Hyg. **46**: 185 (Sept.) 1947.

6. Young, F. W.: Q Fever in Artesia, California, California Med. **69**: 89 (Aug.) 1948.

7. Shepard, C. C., and Huebner, R. J.: Q Fever in Los Angeles County: Description of Some of Its Epidemiologic Features, Am. J. Pub. Health **38**: 781 (June) 1948.

8. Huebner, R. J.; Jellison, W. L.; Beck, M. D.; Parker, R. R., and Shepard, C. C.: Q Fever Studies in Southern California: I. Recovery of Rickettsia burneti from Raw Milk, Pub. Health Rep. **63**: 214 (Feb. 13) 1948.

9. Lennette, E. H.; Clark, W. H., and Dean, B. H.: Sheep and Goats in the Epidemiology of Q Fever in Northern California, Am. J. Trop. Med. **29**: 527 (July) 1949.

possibility exists that both man and his livestock may acquire the infection from a common source.

In a number of instances goats have been the principal domestic animal to which the patient was exposed. Of a sample of 617 goats to which patients had been exposed, 34 per cent had antibodies. The Rickettsia has also been recovered from the milk of this species.[9] In one small semiurban locality in which sheep or dairy cattle are not raised, 3 cases of Q fever occurred within a short distance of a large commercial goat dairy. Twenty per cent of the 160 goats comprising this dairy were serologically positive for Q fever, and the Rickettsia was isolated from several pools of milk specimens. A fourth person, a resident of an apparently nonendemic area, visited this dairy, drank some of the milk and three weeks later had Q fever.

Further evidence that goats may be a source of infection to man was furnished by the occurrence of several cases of Q fever aboard a vessel transporting goats from the United States to the Far East. From serologic evidence obtained, it is presumed that as high as 40 per cent of these animals may have been infected with C. burnetii.

Although thus far the role of sheep and goats in the epidemiology of Q fever in Northern California has been emphasized, the possibility that dairy cattle may be involved was not overlooked; in general, however, few human infections were found to be associated with dairy cattle, and in these instances the proportion of serologically positive cows was small in comparison to the proportion of positive animals of other species.

Nevertheless, in one area where dairying is a major industry, and where sheep are few, 29 human infections with Q fever occurred over roughly a 10 week period. None of these patients had had contact with sheep or goats, one half had had contact with dairy cattle and the majority of the remaining half had had incidental or casual contact (delivery of feed, visits to auction yards, transportation of milk and business calls) with dairies or dairy animals. The Rickettsia was found in pooled raw milk specimens from several producers in this area, and a high proportion of the animals comprising the herds from which these specimens were obtained was serologically positive. Instances such as this, however, in which human beings with Q fever are epidemiologically associated with dairy cattle, appear thus far to constitute an unusual situation in Northern California.

From these considerations it appears that human infection in Northern California is somehow related to more or less direct contact with one or another of three species of domestic livestock, sheep, goats or cattle. It would seem, however, that the problem is somewhat more subtle. For example, in one rural town of 3,000 population, 41 cases of Q fever occurred over a period of 11 weeks; 37 of these persons had had no direct contact with livestock of any kind. All but two patients were men, the age range being from 19 to 82 years. The 39 men represented a wide diversity of urban occupations; it is interesting to note that eight were county employees or attorneys who spent all or most of their working hours in one building. None of the 41 patients appeared to have contracted the illness from another person, although many of them had some degree of contact with one another. In the vicinity of the town there were nine small dairy herds. From eight of these, 195 cows were tested for complement-fixing antibodies and all were negative. More than 20,000 sheep were present in the grazing areas lying on either side of the town; 446 blood specimens were taken from sheep in the 13 flocks comprising this total, and 47 (10.5 per cent) were serologically positive.

### ENVIRONMENTAL ROUTES OF INFECTION

Epidemiological studies [10] of this outbreak have provided no satisfactory answer concerning the sources and routes of infection. However, the recovery, in the course of other studies, of the Rickettsiae in the secretions and/or excreta of sheep, goats and cattle led us to speculate on the potentialities of infection arising from an infected environment. In the outbreak under discussion it was found that serologically positive sheep were present in the area and that a number of these animals had been driven or trucked through the town. Further, the outbreak occurred at the time of year when movement and handling of the animals is at a maximum because of lambing, shearing and changing of grazing areas.

There exists the possibility that contaminated fields and roadways may serve as loci for air-borne dissemination of the Rickettsia. Similarly, contamination of the clothing of those persons handling sheep may have been a means of transporting the Rickettsia to its victims. Neither of these speculations, however, accounts satisfactorily for the evident disproportion between the numbers of male and female patients. Other possible sources of infection, such as water, food, milk and domestic mosquitos, common in general to both males and females, provided equally unsatisfactory explanations.

In at least one other instance a similar but smaller outbreak occurred in an urban area where contact with domestic livestock was also infrequent. The age, sex and occupational distribution of patients were comparable to that mentioned for the outbreak discussed above. In this instance, too, it was not possible to ascertain the sources and routes of infection involved, but advantage was taken of this outbreak to study the possibility of person to person or familial transmission. Among the 20 persons involved in this outbreak, there was no evidence of more than the most casual contact between one person and another. A total of 37 familial contacts of these patients was investigated for evidence of apparent or inapparent infection with C. burnetii. Although none of these was found to have had a frank illness during the period of this outbreak, two of these familial contacts had complement-fixing antibodies. Both were women; one laundered clothing soiled with excreta of sheep and cattle, the other frequently rode horseback through fields where sheep were pastured. The observations in this small group would seem to support the impression that person to person transmission of infection is uncommon.

10. Clark, W. H., and co-workers: To be published.

### INCIDENCE OF Q FEVER

It should not be assumed from what has been said above that Q fever in California has occurred only in epidemic form and only in certain areas. During the two years covered by the studies in Northern and Southern California, more than 700 cases have been uncovered in the state; what the true incidence may be is still unknown. The disease has been found to occur in at least 29 counties of California (24 of these counties lie north of the Tehachapi Range), and in many of these counties the disease is now known to be endemic. The recent publications by Beck and associates [11] and by Bell and others [12] have summarized well what is presently known of the epidemiology of the disease in Southern California.

In Northern California, the 48 counties lying, in general, north of the Tehachapi Mountains, nearly 450 cases of Q fever have been confirmed by our laboratory. Of these, adequate epidemiological records are available for 350. The data thus far obtained indicate that the disease is seasonal in its occurrence; nearly 70 per cent of the cases occurred during the months of March, April and May. The incidence is at a minimum during the late autumn months.

The age of the patients ranged from 9 to 87 years, with the majority of the patients falling into the age group 20 to 49 years. The ratio of males to females was 10: 1. The occupations have been representative of those found in any agricultural community and in addition include such nonagricultural pursuits as store manager, bartender, card dealer and attorney.

Of the 350 patients, 77 (22 per cent) were users of raw milk; since the majority of these 350 patients lived in primarily rural areas, this proportion of raw milk users does not appear to be inconsistent with the expected proportion of consumers of unpasteurized milk in such areas. In an occasional instance, however, ingestion of raw milk has appeared to be a possible explanation for the occurrence of the illness.

Contact with domestic livestock was relatively frequent, as might be expected in an area devoted to agriculture; thus, of 350 patients, 189 (54 per cent) were known to have had contact with sheep, goats or cattle at their place of occupation. Of the 161 persons who did not come into contact with animals at their place of occupation, 53 (33 per cent) were exposed to contact with livestock at their place of residence. Thus, of the entire series, 242 patients (69 per cent) had had more than casual contact with livestock.

### COMMENT

In Northern California, as in Southern California and elsewhere, the sources of infection and modes of transmission of Q fever to man have not been clearly defined. In 18 months of study in Northern California, however, there is evidence that domestic livestock are involved in the epidemiology of the human disease, although a causal relationship has not been established. The occurrence of the infection in primarily agricultural areas, rural or urban, the close association of a high proportion of the recognized cases with domestic livestock and unquestionable evidence that infection with C. burnetii is present in the domestic livestock in those regions where human infections are occurring, all point to domestic animals as a possible source of the Rickettsia.

From the age, sex and local geographic distribution of the cases, it appears unlikely that milk, food or water is commonly the vehicle for the transmission of the disease. The absence of any history of tick bite appears to rule out this arthropod as an important vector of the disease to man; other arthropod species such as the mosquito cannot be as easily excluded. As in the case of jungle yellow fever, natural infection of a species of mosquito whose biologic limitations confine its activities to a narrow range might provide a means of infection of man, which could give rise to an age and sex distribution compatible with that observed for Q fever in Northern California. However, the seasonal peak of the human disease in the early spring months does not coincide with the maximum seasonal prevalence of known mosquitoes in this area. Furthermore, although the numbers tested have been small, no recoveries of the organism have been made from mosquitos.

If it is postulated that domestic livestock may serve as a source of infection for man, direct association with these animals would appear to account for 70 per cent of the human infections observed in Northern California. Contamination of the environment by the excreta and secreta of infected animals would increase the hazard of infection for persons in casual or close contact with livestock and, in addition, would make possible the infection of persons at some distance from the source. Contaminated clothing could carry the infection to those not exposed to livestock.[13] Similarly, infected dust from stock truck beds, stock cars, grain-grinding mills, hay storage sheds and grain stubble used as pasture may serve as a source of infection for persons seldom or never exposed directly to livestock.

That contamination of the environment is possible has been demonstrated by our recovery of C. burnetii from the milk and placentas of naturally infected sheep and from the milk, urine, feces, oral and nasal secretions and placentas of experimentally infected sheep. The presence of the Rickettsia in the dust-laden air of premises harboring infected sheep,[14] dairy cattle [14] and dairy goats [15] has been demonstrated and suggests a possible means of carrying infection to man. In Northern California the seasonal occurrence of cases coincides roughly with the lambing season, a period

11. Beck, M. D.; Bell, J. A.; Shaw, E. W., and Huebner, R. J.: Q Fever Studies in Southern California: II. An Epidemiologic Study of 300 Cases, Pub. Health Rep. 64: 41 (Jan. 14) 1949.

12. Bell, J. A.; Beck, M. D., and Huebner, R. J.: Epidemiologic Studies of Q Fever in Southern California, J. A. M. A. 142: 868 (March 25) 1950.

13. Oliphant, J. W.; Gordon, D. A.; Meis, A., and Parker, R. R.: Q Fever in Laundry Workers: Presumably Transmitted from Contaminated Clothing, Am. J. Hyg. 49: 76 (Jan.) 1949. Beck, Bell, Shaw and Huebner.[11]

14. DeLay, P. D.; Lennette, E. H., and DeOme, K. B.: Q Fever in California: II. Recovery of Coxiella Burnetii from Naturally-Infected Air-Borne Dust, J. Immunol. 65: 211 (Aug.) 1950.

15. Lennette, E. H., and Welsh, H. H.: To be published.

when greatest contamination of the environment might be expected to occur through milk and placentas. By way of comparison, in Southern California, where the dairy herds produce milk the year around (and calving is not seasonal), cases of human Q fever occur throughout the year and a seasonal incidence has not been noted.[11]

SUMMARY

Studies conducted in both Northern and Southern California have shown that a large proportion of patients with Q fever have had exposure to domestic livestock by virtue of either occupation or residence. Contamination of the environment with excreta or secreta of infected animals has been suggested as a means of dissemination of the Rickettsia from animal to man. This finds support in the demonstration of the Rickettsia in these excreta and secreta and recovery of the organisms from dust-laden air of sites on which infected animals were present. Evidence concerning the portal of entry is not conclusive but suggests that human infection may occur through ingestion or inhalation of the Rickettsia.

## ABSTRACT OF DISCUSSION

### On Papers by Drs. Lennette and Clark and Drs. Huebner and Bell

Miss M. Dorthy Beck, Berkeley, Calif.: The complexity of the epidemiology of Q fever in California is emphasized by the papers which have been presented. To date, Q fever has not been included on the list of reportable diseases, even though basic epidemiological data might have been obtained by such a procedure. Q fever was shown to be endemic in the general population for the first time in 1947. Previously, only sporadic outbreaks had been observed. In outbreaks the disease is easier to recognize, and the regulations of the California State Department of Public Health have required for many years the reporting of the unusual occurrence of any disease. The sporadic case, on the other hand, is clinically difficult to diagnose. Without laboratory confirmation, cases of influenza, pneumonia and even brucellosis, psittacosis or typhus might be included. Epidemiological history regarding exposure of the patient to presently known sources of Q fever may be of some assistance to the physician in determining which group of diseases is involved, as in 70 to 80 per cent of the known cases in California there is a history of such exposures. This may permit better use of the laboratory to obtain a definitive diagnosis, even though in retrospect. Since only a few laboratories in California are equipped to do the necessary tests, it has been possible to obtain a crude but usable index of the incidence of Q fever without requiring reporting. Eventually reporting may be considered necessary, when our knowledge of the disease is more complete. With regard to the pasteurization of all milk, the effectiveness of such a control procedure alone must be immediately questioned when the multiple sources of spread are considered. A high percentage of positive complement fixation reactions for Q fever was obtained from those who used raw milk in their households but did not work or live in or near dairies. Although pasteurization would seem to be sufficient protection for this group, they constitute only one third of the cases investigated. Additional evidence showed that persons intensely exposed to raw milk only on the job also had a high percentage of positive serologic reactions. Pasteurization could not reduce infections in this group even though vaccination of humans and animals might. Again, in the area surveys, the percentage of positives was increased when the only possible exposure was residence near dairies. Prevention of infection in such a group would require their change of residence or the removal of the dairies from the urban areas. Obviously, therefore, pasteurization as the single measure of control would have a limited effect on preventing Q fever. The only conclusion, which can be reached is that for effective control efforts must be directed against the major animal sources of human infection—dairy cows, sheep and goats. To do this, additional basic information must be obtained on the mode or modes of transmission of infection and the effect of vaccination in these animals.

Mr. Hartwell H. Welsh, Berkeley, Calif.: Q fever is often eliminated as a possibility in differential diagnosis when a patient's history fails to elicit a positive response to the query, "Have you had any contact with livestock or livestock products?" Dr. Lennette has pointed out, as have others, that although contact with livestock can be considered to be an epidemiological factor of great importance in a majority of the cases, there are a large number of infections which cannot be explained on this basis. Dr. Lennette has spoken of an outbreak occurring on the campus of a college of agriculture in which 70 cases occurred. Direct contact with domestic animals was not definitely established in many of these cases. Likewise, of 41 cases in a rural town of 3,000 population only four patients had had any direct contact with livestock. A similar situation was shown to exist in another community. As Miss Beck has stated, approximately 70 to 80 per cent of the cases studied in Southern California could be related in some manner to domestic livestock. The remaining 20 to 30 per cent are unexplained. These figures give rise to an interesting hypothesis, that apparently the etiologic agent of Q fever is capable of surviving transportation over some distance and remains viable for a considerable period of time outside the host. The survival of other Rickettsiae is a matter of record. Its resistance to desiccation, heat and chemical agents has recently been reported by Dr. Huebner in a paper on "Thermal and Chemical Resistance of Coxiella Burnetii" read before the fiftieth general meeting of the Society of American Bacteriologists, Baltimore, May 14-18, 1950. Therefore, persons not normally thought of as being exposed to what is considered the primary source of the disease, livestock, may well be exposed to infection through the medium of a contaminated atmosphere or through contact with the contaminated clothing or person of individuals who have been in direct contact with the accepted sources of infection. Oliphant, Gordon, Meis and Parker have reported on cases of Q fever in laundry workers whose infections were traced to contaminated clothing. Beeman (*Pub. Health. Rep.* 65:88, 1950) has reported two cases in which infections were traced to contact of patients with personal effects of a laboratory worker who lived in their home. Furthermore, examination of the available data concerning cases of Q fever in which there is no evidence of livestock contact reveals that a goodly number of these cases occur in persons whose occupations keep them indoors a large portion of the time. They also come into contact, through the nature of their services, with others whose clothing might well be contaminated. These persons necessarily spend their time in an atmosphere which can be considered relatively static in nature and therefore one in which the etiologic agent could be expected to remain suspended and viable for some time. The occupations covered workers such as bartenders, barbers, store clerks, warehousemen, telephone operators, mechanics, card room operators and players. In view of the accumulating evidence with respect to contaminated air, the possibilities for the spread of Q fever through contaminated atmospheres and clothing of persons who are in contact with livestock to persons other than those whose residence and occupation are suspect is a tenable hypothesis. Physicians therefore must be alert to the possibility of infection with Q fever even when the accepted criteria with respect to livestock contact are lacking, especially in areas where Q fever is known to occur endemically in domestic livestock.

# TUBERCULOUS PERICARDITIS TREATED WITH STREPTOMYCIN

*Abraham Falk, M.D.*
*and*
*Richard V. Ebert, M.D., Minneapolis*

The use of streptomycin in all forms of tuberculosis has been the subject of a clinical study by the Veterans Administration since 1946. During that period streptomycin was used in all clinically recognized cases of tuberculous pericarditis at the hospitals engaged in this study, but results have not been published. Analysis of the clinical data forms the basis of this report. The onset of pericarditis in many of these patients occurred during hospitalization for pulmonary tuberculosis, and in the others hospital admission was secured soon after onset.

## CRITERIA FOR SELECTION OF CASES

Twenty-five cases of proved or presumptive tuberculous pericarditis treated with streptomycin were reviewed. Criteria adequate for the diagnosis of pericarditis and proof of its tuberculous etiology were established, in order that cases of uncertain causation might be eliminated. The diagnosis of pericarditis in this study was not made unless fluid was obtained by pericardial aspiration or histological proof of pericarditis was found in tissue removed at pericardiectomy or autopsy. Tuberculous etiology was proved by bacteriologic demonstration of acid-fast bacilli from the aspirated pericardial fluid by smear, culture or guinea pig inoculation in 14 cases and by histological diagnosis of tuberculosis in pericardial tissue removed at operation in three cases. Extrapericardial tuberculosis was proved in four cases in which the diagnosis could not be proved on the basis of bacteriologic or histological observations but in which definite pericarditis existed in association with other forms of tuberculosis. Four cases were eliminated chiefly for lack of adequate bacteriologic evidence, leaving a total of 21 cases for the study.

## CLINICAL OBSERVATIONS

All 21 patients were male and were almost equally divided between whites (10 patients) and Negroes (11 patients) (table 1).[1] This incidence among Negroes is considerably less than the 2:1 ratio usually reported,[2] but the factor of selection for military service may account for this difference. The age range in this study was 19 to 61 years, with about half the patients grouped in the third decade and the remainder in the sixth and seventh decades. Nineteen patients had pericardial effusion proved by aspiration. The aspirated fluid was either serous, serosanguineous or frankly bloody, and the quantity obtained on one or more aspirations ranged from 20 to 5,000 cc. Tubercle bacilli were found in the fluid in 14 cases. In general, the serous pericardial effusions reflected the usual observations of tuberculous effusion in the serous spaces, as described by Andrews and others[3] and Hannesson.[2b] In two cases no fluid was obtained on aspiration of the pericardial space, and the histories did not indicate previous clinical recognition of effusion or pericarditis. The primary feature in each of these two cases was the insidious onset of circulatory failure, and the etiologic diagnosis was confirmed only after pericardial resection and histological study of the tissue removed.

All 21 patients in this study had circulatory failure. The diagnosis of failure was based either on the observation of a venous pressure above 15.0 cm. of water or increased cervical venous distension (with the patient in the sitting position) in combination with paradoxical pulse, enlarged liver, ascites or peripheral edema. Venous pressure was recorded in 18 of the 21 cases, and was elevated in all except one, in which the clinical picture was characteristic of circulatory failure. Roentgenograms of the chest were obtained in all cases and revealed enlargement of the cardiac silhouette. Cardiac fluoroscopic or roentgenkymographic studies were done in half the cases and revealed decidedly diminished or absent cardiac pulsations in all instances.

Electrocardiographic changes consisted of lowering of the QRS and T waves, with frequent inversion of T in the limb leads and often in CF 4, 5 and 6. The changes were similar to those previously described in the disease.[4] Although the amplitude of QRS returned to normal fairly rapidly after treatment in this series, the T wave changes tended to persist for long periods and in some instances had not returned to normal even several years after all evidence of circulatory failure had subsided. Auricular fibrillation was noted in only one case.

Eighteen patients in this series had pleural effusion, before, during or after the onset of pericarditis; most of the effusions occurred prior to or during the exudative phase of the pericarditis. Acid-fast bacilli were isolated from the fluid in only five cases, but bacteriologic studies were not invariably done. It is likely that in most instances the pleural effusion was a manifestation of tuberculosis rather than of circulatory failure.

## PRIMARY TREATMENT WITH STREPTOMYCIN

Of the 19 patients with proved pericardial effusion, 17 were treated primarily with streptomycin. In addition, they received bed rest, pericardial aspirations, digitalis, low salt diet and diuretics. The dosage and duration of streptomycin treatment varied considerably (table 2), reflecting the regimens recommended by then

From the Department of Medicine, University of Minnesota Medical School and the Veterans Administration Hospital, Minneapolis.

Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

The Streptomycin Committees and Staffs of the following Veterans Administration Hospitals supplied the clinical data for this study: Brecksville, Ohio; Butler, Pa.; Castle Point, N. Y.; Cleveland; Columbia, S. C.; Dearborn, Mich.; Hines, Ill.; Kennedy Veterans Administration Hospital, Memphis, Tenn.; Louisville, Ky.; McKinney, Texas; Minneapolis; Oteen, N. C.; Swannanoa, N. C., and Tucson, Ariz.

1. Table 1 is omitted from THE JOURNAL because of lack of space, but it is included in the authors' reprints.

2. (*a*) Harvey, A. M., and Whitehill, M. R.: Tuberculous Pericarditis, Medicine **16**: 45 (Feb.) 1937. (*b*) Hannesson, H.: Tuberculosis of the Pericardium and Heart, Tubercle **22**: 79 (April) 1941.

3. Andrews, G. W. S.; Pickering, G. W., and Sellors, T. H.: The Ætiology of Constrictive Pericarditis, with Special Reference to Tuberculous Pericarditis, Together with Note on Polyserositis, Quart. J. Med. **17**: 291 (Oct.) 1948.

4. (*a*) Harvey and Whitehill.[2a] (*b*) White, P. D.: Chronic Constrictive Pericarditis (Pick's Disease) Treated by Pericardial Resection, Lancet **2**: 539 (Sept 7); **2**: 597 (Sept. 14) 1935.

current Veterans Administration treatment protocols. The majority of the patients received 1 to 2 Gm. of streptomycin daily over a period of 60 to 120 days. Three patients received additional short courses of streptomycin during or after subsequent pericardiectomy. Two patients received intrapericardial instillations of streptomycin in addition to intramuscular therapy; one (G. R.) was given 0.5 Gm. daily for 17 days and the other (J. Co.) received 0.3 Gm. daily for six days. No untoward reactions occurred with this local therapy.

The symptoms of circulatory failure improved or disappeared after treatment with streptomycin was started in eight of the 17 cases (table 2). In the remainder streptomycin therapy had no influence on these symptoms. Of the eight patients who responded to therapy one died subsequently of tuberculous meningitis. The remainder of the patients with a favorable response have been followed five to 24 months and have had no recurrence of symptoms of circulatory failure, although all are still hospitalized for treatment of extrapericardial tuberculosis.

Of the nine patients who did not respond to streptomycin therapy five died subsequently; one died of tuberculous meningitis, one of miliary tuberculosis, two probably of air embolus and one, who refused pericardiectomy, of circulatory failure. Of the remaining four patients in this group, three subsequently underwent pericardiectomy for relief of constrictive pericarditis, and the fourth is awaiting pericardiectomy. Of the three patients subjected to pericardiectomy, two had relief of symptoms and the third died in the immediate postoperative period (table 3).

Streptomycin did not prevent the onset of tuberculous complications in a number of those patients receiving primary streptomycin therapy. In one patient (R. G.) tuberculous meningitis developed approximately 13 months after completion of a course of 2 Gm. of streptomycin daily for 110 days. In another patient (M. J.) miliary tuberculosis developed 14 months after completion of a course of 2 Gm. of streptomycin daily for 60 days. Both died, in spite of additional streptomycin therapy, within a week of the clinical diagnosis of the tuberculous exacerbation. Each had active pulmonary tuberculosis, and neither had responded to the initial course of streptomycin directed toward the pericarditis with circulatory failure. In a third patient (K. G.), who had shown considerable improvement in pericarditis and circulatory failure during a course of 2 Gm. of streptomycin daily for 134 days, tuberculous meningitis developed within 14 days of completion of the initial course. Despite an additional course of streptomycin, the patient died approximately seven months later of severe residuals of tuberculous meningitis. It is of interest that tuberculous meningitis developed in this patient within such a short period following completion of therapy.

TABLE 2.—*Results of Treatment of Pericardial Effusion with Circulatory Failure Employing Streptomycin as Primary Therapy*

| Patient | Duration of CF* Prior to Streptomycin, Days | Streptomycin | | Subsidence of CF* After Streptomycin† | Post-Treatment Status | | Follow-Up † |
|---|---|---|---|---|---|---|---|
| | | Dose, Gm. | Duration, Days | | Circ. Status | Complications | |
| A. M. | 21 | 1 | 120 | 2 mo. | Normal | Chest abscess | 29 mo.—Living |
| J. S. | 14 | 1 | 42 | 1 mo. | Normal | Pleural eff. | 8 mo.—Living |
| A. W. | 30 | 1 | 120 | 3 mo. | Normal | None | 18 mo.—Living |
| H. H. | 10 | 2 | 42 | 1 mo. | Normal | Chest abscess | 13 mo.—Living |
| J. G. | 2 | 1 | 42 | 2 weeks | Normal | Tbc. adenitis | 5 mo.—Living |
| J. R. | 30 | 2 | 120 | 3 mo. | Normal | None | 24 mo.—Living |
| K. G. | 60 | 2 | 134 | 4 mo. | Normal | Tbc. meningitis | 12 mo.—Dead |
| J. Co. | 7 | 1 | 53 | 1½ mo. | Improved | None | 17 mo.—Living |
| G. S. | 14 | 1 | 80 | Unchanged | Worse | Circ. failure | 17 mo.—Living |
| G. R. | 10 | 1 | 120 | Unchanged | Unchanged | Air embolus | 7 mo.—Dead |
| M. J. | 60 | 2 | 60 | Unchanged | Unchanged | Miliary tbc. | 7 mo.—Dead |
| R. G. | 30 | 2 | 110 | Unchanged | Worse | Tbc. meningitis | 16 mo.—Dead |
| T. G. | 14 | 2 | 131 | Unchanged | Worse | Circ. failure | 12 mo.—Dead |
| F. B. | 4 | 1 | 54 | Worse | Worse | Air embolus | 4 mo.—Dead |
| E. G. | 60 | 1 | 42 | Unchanged | Subsequent pericardiectomy ‡ | | |
| D. K. | 14 | 1 | 120 | Unchanged | Subsequent pericardiectomy ‡ | | |
| J. Ca. | 30 | 2 | 25 | Unchanged | Subsequent pericardiectomy ‡ | | |

* Circulatory failure.
† From start of streptomycin therapy.
‡ See table 3.

An exacerbation of tuberculous adenitis developed in one patient; a tuberculous abscess of the chest wall occurred at aspiration sites in two, and a tuberculous pleural effusion followed the completion of streptomycin therapy in one. In all four, there was clinical subsidence of pericarditis and circulatory failure with the initial streptomycin therapy. The complications in this group have responded, or are responding, to additional streptomycin therapy. There was no difference in the incidence of complications in either racial group and no evidence of extension of pulmonary disease during or after streptomycin therapy in any of the cases.

### RESULTS OF STREPTOMYCIN THERAPY AS ADJUNCT TO PERICARDIECTOMY

Four patients, two with and two without known pericardial effusion, had pericardiectomy as primary treatment (table 3). Streptomycin was given as an adjunct during or after the surgical period. Circulatory failure had existed an average of five months prior to surgical treatment. The symptoms of circulatory failure were relieved in all patients. Two of these have been the

subjects of reports in the literature [5]; in one of them (J. B.) there was considerable difficulty in control of the circulatory failure following pericardial resection. Three of the four patients in this group are classed as cured and are working or able to work. The fourth, age 56, is considerably improved but requires digitoxin for control of mild circulatory failure. No tuberculous complications or exacerbations occurred in this group after operation.

### PATHOLOGY OF PERICARDIAL TISSUE REMOVED AT OPERATION OR AT AUTOPSY

Histological studies were carried out on pericardial tissue from nine patients. Three of these were subjected to operations after they had failed to respond to streptomycin alone. In two of the three (J. Ca. and D. K.), active tuberculous lesions were found in the resected tissue, five and six months, respectively, after the beginning of treatment with streptomycin. The remaining patient (E. G.) received a course of streptomycin two months prior to pericardiectomy and had only nonspecific inflammatory changes in the pericardial tissue, although postmortem examination revealed extensive tuberculous involvement of the mediastinal and tracheobronchial lymph nodes, with only a minimal and probably inactive lesion in the upper lobe of the right lung.

TABLE 3.—*Results of Pericardiectomy*

| Patient | Duration CF* Preoperatively | Streptomycin: Dose, Gm. | Streptomycin: Duration, Days | Duration CF* Postoperatively | Present Status: Result | Present Status: Follow-Up |
|---|---|---|---|---|---|---|
| **Pericardiectomy as Primary Therapy** | | | | | | |
| J. B. | 9 mo. | 2 | 60 | 3 mo. | Cured | 2 yr. |
| F. I. | 4 mo. | 2 | 120 | 5 mo. | Cured | 2 yr. |
| L. S. | 5 mo. | 2 | 45 | 4 mo. | Cured | 1 yr.† |
| S. S. | 1 mo. | 1 | 12 | 1 mo. | Improved | 1 yr. |
| **Pericardiectomy in Primary Streptomycin Treatment Failures** | | | | | | |
| J. Ca. | 6 mo. | 2 | 25‡ | 3 mo. | Cured | 2½ yr. |
| D. K. | 7 mo. | 1 | 10‡ | 1 mo. | Improved | 4 mo. |
| E. G. | 5 mo. | 1 | 11‡ | Died | Died 4 days after operation | |

* Circulation failure
† Lost to follow-up one year after operation.
‡ Additional streptomycin during operation.

Autopsies were done on two of the six patients who received primary streptomycin therapy and died without surgical treatment. The first patient (M. J.) had only nonspecific inflammatory changes in the pericardial tissue without histological evidence of tuberculous foci or reaction; he had shown no response to streptomycin therapy from the standpoint of improvement of circulatory failure. The other (T. G.) had histological evidence of tuberculous granulomas in portions of the pericardium, with tubercle bacilli demonstrable by acid-fast staining 12 months after the start of streptomycin therapy. Death was due to severe circulatory failure after the patient refused pericardiectomy. In each of these cases there was extensive pericardial thickening and adherence of the pericardium to the heart, as well as evidence of extrapericardial tuberculosis.

The four patients who were subjected to primary pericardiectomy, without previous courses of streptomycin, were all found to have evidence of active tuberculous pericarditis. Calcification of the pericardium was not found at operation in any of the cases.

The eventual hyalinization of fibrous tissue and the disappearance of caseous foci and other evidences of tuberculous involvement, or the persistence of cavities or pockets containing only inspissated caseous debris, may leave a pericardial lesion without specific histological or bacteriologic identity.[6] Such changes have been noted in instances in which the tuberculous etiology had been proved by bacteriologic study of aspirated fluid from pericardial effusion early in the process and probably account, in some degree, for our difficulty in determining the causative factors of many cases of constrictive pericarditis. The effect of streptomycin on the healing of the pericardial lesions in our series cannot be well evaluated, in view of the few cases observed and of the known fact that healing may occur without specific therapy.

### COMMENT

It is apparent that tuberculous pericarditis is a complex disease with a variable clinical course, and any evaluation of therapy must be tempered with caution. A review of the natural course of the disease is necessary before conclusions can be made. Pericardial effusion is an almost constant feature in the early stage of tuberculous pericarditis, and the presence of fluid in the pericardium frequently produces cardiac tamponade with resultant circulatory failure. Death may ensue in this stage of the disease if the mechanical interference with cardiac function is not relieved by aspiration. The pericardial effusion disappears in time, but frequently a thick wall of tuberculous granulation tissue is left, encasing the heart and limiting its function. This may eventually heal, leaving dense fibrous tissue without evidence of tuberculosis. The term constrictive pericarditis has been used to describe circulatory failure caused by encasement of the heart by a thickened pericardium. It is believed by many that most cases of constrictive pericarditis are of tuberculous origin, even though the fibrous tissue surrounding the heart shows no pathological evidence of this causation. Finally, tuberculous pericarditis is commonly associated with serous extrapericardial tuberculosis. Death may occur from the associated tuberculosis or from miliary spread.

A statistical evaluation of the natural course of the disease is difficult to obtain. Perhaps the best data available are in a recent report by Andrews, Pickering and Sellors.[3] These authors studied 18 patients with tuberculous pericarditis, all of whom were seen during the stage of pericardial effusion with grossly elevated venous pressure and enlargement of the liver. At the time of the conclusion of the study 10 of the 18 patients were dead. Of the eight living patients, six had been subjected to pericardiectomy.

Often the diagnosis of tuberculous pericarditis cannot be proved except at operation or autopsy, which is one of the difficulties in evaluation of statistics. The col-

5. Moore, J. A., and Murphy, J. D.: Constrictive Pericarditis with Tuberculous Intrapericardial Abscess Treated with Streptomycin: Report of a Case, Ann. Surg. **127**: 685 (April) 1948. Hughes, F., and Lipton, S.: Chronic Constrictive Tuberculous Pericarditis, Dis. of Chest **16**: 66 (July) 1949.

6. Blalock, A., and Levy, S. E.: Tuberculous Pericarditis, J. Thoracic Surg. **7**: 132 (Dec.) 1937.

lection of cases from Johns Hopkins Hospital reported by Harvey and Whitehill [2a] illustrates this. Of 20 patients with proved tuberculous pericarditis with effusion, 80 per cent died; of 17 patients with proved tuberculous pericarditis without effusion, 83 per cent died. The causative factor in most of these cases was established at autopsy. On the other hand, there were 34 cases in which a clinical diagnosis of tuberculous pericarditis was made but proof of causation was not obtainable. The mortality was only 5.9 per cent in this group. A review of the case summaries indicates that many of the latter group did, in fact, have tuberculous pericarditis. The diagnosis is particularly certain in those patients with proved extrapericardial tuberculosis. Blalock and Levy [6] report their cases in a similar manner. In their series, 20 of the 24 patients with proved tuberculous pericarditis died. Three of the living patients had been subjected to pericardiectomy. Of the 18 patients in whom tuberculous pericarditis was strongly suspected but not proved, eight died. In the series of cases of tuberculous pericarditis reported by Keefer [7] and by Fenger and Hansen,[8] both the mortality and the number of autopsies were high. In the latter series the disease was diagnosed at autopsy without clinical recognition in 16 cases; of the six cases in which clinical diagnosis was made, death occurred in three. Thus, the mortality rate was 88 per cent for the entire series and 50 per cent for the cases with clinical diagnosis.

It is obviously extremely difficult for one to determine the mortality rate for tuberculous pericarditis. The criteria used for clinical diagnosis and the inclusion of cases in which the disease is diagnosed at autopsy, but not recognized clinically, strongly influence the death rate in any series of cases. For this reason an ideal study of the effect of therapy on the disease should consist of treatment of alternate cases. This was not done in the present study; hence any conclusions regarding the efficacy of therapy must be drawn with extreme caution.

The effect of streptomycin on the effusion and circulatory failure of tuberculous pericarditis can best be evaluated by comparison of this series with the cases reported by Andrews and others.[3] Of 18 patients with tuberculous pericarditis in the latter series, none of whom received streptomycin, only two (11 per cent) improved with medical management alone. The remaining six survivors improved only after pericardiectomy. In our group of 17 patients, all of whom received primary streptomycin therapy as part of their medical management, eight (47 per cent) demonstrated initial and sustained improvement by subsidence of the pericardial effusion and circulatory failure. The difference between the incidence of improvement in the two series suggests that streptomycin therapy may decrease the incidence of constrictive pericarditis. Unfortunately it is difficult for one to be certain that the two series are comparable. The possibility that constrictive pericarditis may develop in those patients showing an initial response to streptomycin therapy cannot be excluded except by a long term study.

The effect of streptomycin therapy on the mortality was less striking. In Andrews' series [3] the mortality rate was 55 per cent. The mortality rate in our group of 17 patients treated primarily with streptomycin was 35 per cent.

Streptomycin had no appreciable therapeutic effect on the pulmonary tuberculosis, which existed at the start of treatment. Such concomitant pulmonary disease was almost entirely productive or fibrotic, and the response of nonexudative disease to the antibiotic is known to be limited. Existing pleural effusions frequently subsided during therapy, but we cannot attribute this directly to the effect of streptomycin. The most disappointing aspect of streptomycin therapy was the failure of the antibiotic to prevent subsequent miliary spread and the development of tuberculous meningitis. It was largely these complications that led to the high mortality.

Pericardiectomy has offered the only therapeutic approach for the relief of circulatory failure secondary to cardiac constriction. A review of the American series reported prior to 1948 [9] indicates that only 24 patients with active tuberculous pericarditis were subjected to pericardiectomy. Andrews and others [3] reported an additional nine cases from England in 1948. The fear of disseminating tuberculosis by surgical intervention on an active pericardial lesion, the possibility that secondary constriction would result from the residual inflammatory process after pericardiectomy and perhaps the general disinclination of surgeons to operate on patients with active tuberculosis, pericardial or otherwise, may have been factors limiting the surgical approach.[10] Andrews and co-workers [3] and Blalock and Levy [6] do not believe that active pericardial disease should be a contraindication to pericardiectomy when circulatory failure is persistent. In the 33 pericardiectomies reported there have been 16 deaths, only six of which were attributable to disseminated or exacerbated tuberculosis. The remainder were due to the operation itself. In our series of seven pericardiectomies there was only one death, and this was due to surgical treatment. It is apparent that no conclusions can be drawn from this small number of cases. Further studies on the treatment of active tuberculous pericarditis of the constrictive type with streptomycin and early operation are urgently needed.

The relation between the streptomycin regimen and the therapeutic result could not be determined from this study because of the varying dosage and duration of therapy. Continued experience with streptomycin has indicated the greater efficacy of prolonged therapy in most cases of pulmonary and extrapulmonary tuberculosis. The addition of paraaminosalicylic acid has decreased the rate of emergence of streptomycin-resistant tubercle bacilli; a lower dosage of streptomycin has diminished the toxic effects. The present

7. Keefer, C. S.: Tuberculosis of the Pericardium: Study of 20 Cases, Ann. Int. Med. **10**: 1085 (Feb.) 1937.

8. Fenger, E., and Hansen, O. S.: Tuberculous Pericarditis: Incidence at Glen Lake Sanatorium, Minnesota Med. **29**: 326 (April) 1946.

9. (*a*) White.[4b] (*b*) Blalock and Levy.[6] (*c*) Churchill, E. D.: Pericardial Resection in Chronic Constrictive Pericarditis, Ann. Surg. **104**: 516 (Oct.) 1936. (*d*) Heuer, G. J., and Stewart, H. J.: Surgical Treatment of Chronic Constrictive Pericarditis, Surg., Gynec. & Obst. **68**:979 (June) 1939. (*e*) Blalock, A., and Burwell, C. S.: Chronic Pericardial Disease, Surg., Gynec. & Obst. **73**: 433 (Oct.) 1941.

10. Keefer,[7] Churchill,[9c] Beck, C. S.: Report of the Sixty-Third Meeting of the Society of Clinical Surgery, Cleveland, 1936.

Veterans Administration treatment protocols recommend the concurrent administration of 1 Gm. of streptomycin intramuscularly with 12 Gm. of the sodium salt of paraaminosalicylic acid orally daily for 120 days. This regimen is suitable for the treatment of tuberculous pericarditis.

SUMMARY AND CONCLUSIONS

Seventeen patients with tuberculous pericardial effusion and associated circulatory failure were treated primarily with streptomycin. There was disappearance or definite improvement of circulatory failure in eight patients, or 47 per cent. Six, or 35 per cent, of the patients died. Patients failing to respond to primary streptomycin treatment may be relieved of symptoms by pericardiectomy. The influence of streptomycin on mortality was not dramatic, largely because the antibiotic failed to prevent subsequent miliary or meningeal tuberculosis. Streptomycin was used as an adjunct to surgical treatment for active tuberculous pericarditis in four patients, and operation was performed after primary streptomycin therapy in three cases. There was no spread of the tuberculosis following operation in any case.

## CANCER DETECTION IN RURAL PRACTICE

### REPORT OF 1,650 EXAMINATIONS

*A. C. Siddall, M.D., Oberlin, Ohio*

This report presents the results of a program of cancer detection in rural practice. Sixteen hundred and fifty examinations have been carried out on 950 presumably well women over a period of six years, and 13 malignant growths have been found.

The first cancer detection clinic in this country was established in 1937,[1] and today approximately 240 detection centers are in operation.[2] The Lorain County Medical Society of Ohio fell in line with this movement and opened a detection center in Elyria in 1946 along with a diagnostic clinic in Lorain. For various reasons the county medical society discontinued the Elyria detection center one year ago and, instead, sponsored a program to make every physician's office a cancer detection center. The local cancer committee was to continue with its program of education and publicity. To date 42 members of the county society have signified their willingness to cooperate by giving a complete physical examination for this purpose. Therefore, this is an opportune time for some report to be made concerning the progress of cancer detection in private practice.

It is not difficult for the physician in his office to meet the needs for cancer detection because the two essential requirements laid down by the American College of Surgeons in 1946 were as follows: 1. The equipment shall be adequate for a complete physical examination. 2. Complete records of examinees, which shall include identification data, occupation, history, physical examination and summary, shall be maintained.

The examinees who comprise this study have been encouraged to follow the widely accepted plan of an annual examination followed in six months by a pelvis-breast examination for those 35 years of age and above. The laboratory procedures used included urinalysis, erythrocyte and leukocyte counts, hemoglobin determinations, and, when indicated or when possible, the Kahn test and the cervical spread or cytological smear according to the method of Papanicolaou.[3] No women are included in this detection series who presented signs and symptoms of cancer at the time of the first examination. No women are included who came to the office only for a pelvic examination unless they had previously had a complete physical examination. Final diagnosis of cancer depended on biopsy. In this series of examinees for detection of cancer 105 biopsies were taken, including 66 biopsies of the cervix uteri, 22 of the endometrium, 12 of the breast and five of the skin. Sustained interest in this program is indicated by the fact that the number of return visits has steadily increased. The return visits of the examinees have been for a complete or for a pelvis-breast examination as shown in table 1.

Of the 13 malignant growths found during these 1,650 examinations, the most frequent site of cancer was the breast. The location of these cancers is indicated in table 2.

Less than half of the examinees here reported were 40 years of age and above, yet 84 per cent of the cancers found were in this older age group. The age distribution of the examinees and those with cancer is shown in tables 3 and 4.

In this report the carcinoma of the uterus and three carcinomas of the breast occurred in women who had borne children. The social status and parity are summarized in table 5.

The cervical spread or cytological smear according to the method of Papanicolaou is regarded as a valuable screening method in the search for carcinoma of the cervix and body of the uterus. This method therefore has been utilized, and 200 such smears have been made during the past two years on 188 examinees. All of these smears have been reported negative for malignant cells. Likewise no cancer was found in these same examinees; therefore the procedure has been reliable to date.

The examinee with endometrial carcinoma in this detection series was a 53 year old white biparous woman. Her second examination was done one year after the first and 11 months after the onset of the menopause, and her complaint was uterine bleeding for four months. The final diagnosis was a well differentiated adenocarcinoma of the endometrium with metastasis to both ovaries and the right tube. Treatment consisted of total hysterectomy and bilateral salpingo-oophorectomy. Postoperative radiation was refused, and recurrence in the cul-de-sac was evident

1. L'Esperance, E. S.: Cancer Prevention Clinics, M. Woman's J. 51:17 (Jan.) 1944.
2. Conference on Cancer Detection, Portsmouth, N. H., 1949, New York, American Cancer Society, Inc., 1949.
3. Papanicolaou, G. N., and Traut, H. F.: Diagnosis of Uterine Cancer by the Vaginal Smear, New York, Commonwealth Fund, 1943.

two years following the operation. Two courses of roentgen irradiation have since been given, and the patient is fairly comfortable. The survival time to date is four years.

The four examinees with carcinoma of the breast were treated by radical mastectomy followed by roentgen irradiation. They are all living after a survival time of 5 years, 4 years, 3 years and 1½ years respectively. Recurrence has occurred in only one patient.

Of the three examinees with carcinoma of the bowel, two were deceased after two years and four months respectively. One examinee is well five years after resection of the sigmoid colon.

The youngest examinee in the group with cancer was a white married woman six months post partum who complained of weakness and bleeding gums. Blood examination revealed acute monocytic leukemia. The survival period was only three weeks.

TABLE 1.—*First and Return Visits*

| Year | Complete Examination: First Visit | Complete Examination: Return Visit | Return Visit (Pelvis-Breast Examination) | Total Return Visits | Total Examinations |
|---|---|---|---|---|---|
| 1944 | 196 | 0 | 0 | 0 | 196 |
| 1945 | 187 | 55 | 10 | 65 | 252 |
| 1946 | 249 | 113 | 16 | 129 | 378 |
| 1947 | 133 | 136 | 25 | 161 | 294 |
| 1948 | 92 | 140 | 33 | 173 | 265 |
| 1949 | 93 | 133 | 39 | 172 | 265 |
| Totals | 950 | 577 | 123 | 700 | 1,650 |

TABLE 2.—*Location of Cancers in Detection Group**

| Location | Number of Cancers |
|---|---|
| Fundus uteri | 1 |
| Breast | 4 |
| Bowel | 3 |
| Lymph nodes (Hodgkin's disease) | 1 |
| Blood (leukemia) | 1 |
| Skin | 3 |
| Total | 13 |

* Presumably well women.

Another examinee with a fatal outcome was a white married biparous woman, 36 years of age. The complaint was a small lump in the right inguinal region. Repeated biopsy revealed only chronic lymphadenitis and roentgen therapy was given. However the patient died three years after onset with a typical picture of Hodgkin's disease.

Although this essay is concerned chiefly with the detection of cancer in presumably well women, in private practice patients come to the office with signs and symptoms of possible cancer at the time of the first visit. These patients present a problem of diagnosis. For the purpose of comparison table 6 is included to show 13 more cancers that have been diagnosed in six years, in addition to a like number mentioned above in the detection group. The striking difference between these two groups is that in the detection series the highest incidence of cancer is in the breast while in the diagnostic group the highest incidence is in the uterus. Therefore, in searching for cancer in the apparently well woman, the breast should never be neglected.

The cytological smear has also been used in the diagnostic group, and in two recent cases of obvious carcinoma of the cervix uteri many malignant cells were found. However in one case of postmenopausal bleeding the cytological smear showed no malignant cells while the uterine curettings revealed a well differentiated adenocarcinoma of the endometrium. This demonstrates that a final diagnosis must depend on the biopsy.

TABLE 3.—*Age Distribution*

| Year | No. of First Visits | No. of Patients Examined: Under 30 Yr. | 30-39 | 40-49 | 50-59 | 60-Over | No. of Cancers |
|---|---|---|---|---|---|---|---|
| 1944 | 196 | 56 | 44 | 40 | 29 | 27 | 3 |
| 1945 | 187 | 52 | 37 | 30 | 38 | 21 | 2 |
| 1946 | 249 | 94 | 52 | 30 | 34 | 29 | 2 |
| 1947 | 133 | 62 | 25 | 24 | 14 | 8 | 3 |
| 1948 | 92 | 32 | 21 | 16 | 12 | 11 | 2 |
| 1949 | 93 | 30 | 21 | 16 | 6 | 11 | 1 |
| Totals | 950 | 335 | 200 | 174 | 133 | 107 | 13 |

TABLE 4.—*Age Distribution of Cancers in Detection Group*

| Age, Yr. | Number of Cases |
|---|---|
| Under 30 | 1 |
| 30-39 | 1 |
| 40-49 | 1 |
| 50-59 | 5 |
| 60 and over | 5 |
| Total | 13 |

In the diagnostic group five patients are deceased, one could not be followed and the cases of five more of interest are summarized below.

## REPORT OF CASES

CASE 1.—A nulliparous Negro woman, 56 years of age, complained of a lump which had been present for 5 months on the right side of the vulva. The diagnosis was a well differentiated squamous cell carcinoma of the vulva. Treatment consisted of vulvectomy, bilateral inguinal lymph node resection and roentgen irradiation. There was no recurrence after eight months.

TABLE 5.—*Social Status and Parity*

| | Number of Cases | Number of Cancers |
|---|---|---|
| Parous married | 527 | 10 |
| Nulliparous married | 201 | 1 |
| Nulliparous single | 102 | 2 |
| Totals | 950 | 13 |

TABLE 6.—*Location of Cancers in Diagnostic Group**

| Location | Number of Cancers |
|---|---|
| Cervix uteri | 5 |
| Corpus uteri | 1 |
| Ovary | 1 |
| Vulva | 1 |
| Breast | 2 |
| Bowel | 1 |
| Skin | 2 |
| Total | 13 |

* Patients with symptoms on first visit.

CASE 2.—A white married quadriparous woman 68 years of age, 20 years after the menopause, complained of slight uterine bleeding for six months. The diagnosis was well differentiated adenocarcinoma of the endometrium. Treatment con-

sisted of radium application (4,230 mg.-hr.), total hysterectomy and bilateral salpingo-oophorectomy and roentgen irradiation. There was no recurrence after 17 months.

CASE 3.—A white married nulliparous woman, 42 years of age, complained of slight uterine bleeding for six weeks. The diagnosis was highly anaplastic squamous cell carcinoma of the cervix. She was treated with radium (6,400 mg.-hr.) and roentgen irradiation. The carcinoma had not recurred after three months.

CASE 4.—A Negro single nulliparous woman, 39 years of age, complained of dull lower abdominal pain for five weeks and spotting of blood for one week. The diagnosis was poorly differentiated squamous cell carcinoma of the cervix. Treatment consisted of radium application (6,000 mg.-hr.) and roentgen irradiation. There was no recurrence after two years and ten months.

CASE 5.—A white married uniparous woman, 74 years of age, complained of some enlargement of the abdomen for two months. The diagnosis was pseudomucinous cystadenocarcinoma of the right ovary. The treatment was excision and roentgen irradiation. The uterus and left tube and ovary had been removed 30 years previously. There was no recurrence after 11 months.

TABLE 7.—*Type and Location of Benign Lesions*

| Lesion | Number of Cases |
|---|---|
| Condyloma acuminata | 1 |
| Vulvitis | 3 |
| Bartholin cyst | 1 |
| Hidradenoma | 1 |
| Urethral caruncle | 3 |
| Vaginitis | 4 |
| Gartner's duct cyst | 3 |
| Cervicitis (erosion) | 98 |
| Cervical polyp | 25 |
| Cervical fibromyoma | 1 |
| Uterine fibromyoma | 31 |
| Uterine polyp | 1 |
| Endometriosis | 7 |
| Cystic tumors of ovary | 11 |
| Tuberculous salpingitis | 1 |
| Cystic mastitis | 39 |
| Fibroma and lipoma of breast | 2 |
| Adenoma of thyroid | 23 |
| Total | 255 |

With regard to the detection series, repeated examination of 950 presumably well women over the past six years revealed not only 13 malignant conditions but 255 benign lesions as well. These benign lesions are enumerated in table 7. The patients with cervicitis were treated with cauterization. Approximately half of the examinees with uterine fibromyoma have submitted to surgery as have four patients with ovarian cysts (one dermoid, two pseudomucinous, one serous papillomatous) and one patient with tuberculous salpingitis.

4. Cancer Detection Centers Which Are Approved by the College, Bull. Am. Coll. Surgeons **33**: 1 (Dec.) 1948.

5. The Hillsdale Plan for Tumor Detection, Hillsdale, Mich., 1948.

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7. Howson, J. Y., and Montgomery, T. L.: An Attack upon the Delay Period in Diagnosis of Pelvic Cancer, Am. J. Obst. & Gynec. **57**: 1098 (June) 1949.

8. Meigs, J. V.; Parsons, L., and Nathanson, I. T.: Retroperitoneal Lymph Node Dissection in Cancer of the Cervix, Am. J. Obst. & Gynec. **57**: 1087 (June) 1949.

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10. Novak, E., in discussion on Howson and Montgomery.[7]

## COMMENT

The part that the private practitioner should play in cancer detection has been emphasized many times. The American College of Surgeons recognized this in its bulletin of December 1948 [4] where the statement was made "that the doctor's office is the first line of defense and that such doctor's office should be a cancer detection center." The Hillsdale County Medical Society in Michigan was a pioneer two years ago in inaugurating a program of cancer detection in the office of the physician.[5] Three years ago the cancer committee of the Ohio State Medical Association stated that "the ideal cancer detection center is the office of the family physician." In spite of the foregoing emphasis, a review of the literature for the past 10 years does not reveal any report from an individual private practitioner concerning cancer detection in his office. This does not mean that this serious problem is being neglected, but it indicates that it is difficult to find time to assemble data, keep adequate records and to examine thoroughly the apparently well patient.

Lock [6] has recently reiterated the fact that the chance for recovery from cancer is inversely related to the extent of the disease when treatment is instituted; therefore the early diagnosis of cancer is mandatory. A report by Howson [7] clearly shows that the weak spot remaining in the offense against cancer is the period before therapy.

In the detection series mentioned above, the one woman with endometrial carcinoma had reported for examination one year before the diagnosis was made and at that time there was no evidence of the lesion. She failed, however, to report for a six month pelvis-breast examination as advised, and she also delayed calling for an appointment for four months after the onset of uterine bleeding. This delay in therapy is most serious because, as Meigs [8] points out, in 80 per cent of the cases of cancer of the cervix the growth has extended beyond the cervix proper when the patients are first seen. Only education and periodic examination of presumably well women as urged by MacFarlane [9] will eliminate delay in therapy. No doubt Novak [10] is correct in the statement that "efforts at unearthing cancer in its early and favorable stages [point] the way to a wide-open avenue for the saving of many more human lives than are likely to be saved from any surgical or radiotherapeutic improvements in the foreseeable future."

Popular education should stress the fact that over 80 per cent of all cancers can be found by inspection and palpation and this is the reason the private practitioner should be able to detect cancer in his office. Furthermore, the private practitioner is in a better position to allay the fear of cancer and to treat the multitude of benign lesions that are found than is his colleague in a large detection center.

The response of the examinees in returning to the office for repeated examinations for cancer detection indicates a sustained interest in this kind of program. In the United States there are 20,815,000 women over 45 years of age, and every woman in this

cancer age group could be examined once a year if 100,000 practicing physicians would devote just one hour a week to this work.

SUMMARY

During the past six years a cancer detection program has been carried out in rural practice and 1,650 examinations have been done on 950 presumably well women. Thirteen malignant conditions have been discovered: one of the fundus uteri, four of the breast, three of the bowel, three of the skin, one of the blood (leukemia) and one of the lymph nodes (Hodgkin's disease). Two hundred and fifty-five benign lesions have been revealed and treatment given or advised. An additional 13 cases of cancer have been diagnosed in a second group of women who presented signs and symptoms at the time of their first examination: five of the cervix uteri, two of the breast, two of the skin and one of the endometrium, ovary, vulva and bowel respectively.

ADDENDUM

Since this paper was submitted, 218 additional examinations have been made in the cancer detection program and four more cancers found. Thus, to date, a total of 1,868 examinations have been completed.

# CLINICAL NOTES

## MEDITERRANEAN ANEMIA

### REPORT OF CASE IN AN AMERICAN NEGRO

*Angelo E. Dagradi, M.D.*
*Norman Sollod, M.D.*
*and*
*Jackson H. Friedlander, M.D., Northport, N. Y.*

Cooley and Lee in 1925 [1] called attention to a blood dyscrasia occurring in children and characterized by anemia, splenomegaly and the occurrence of peculiar, roentgenologically demonstrable bone changes. It was originally believed that this disease was almost uniformly fatal before the age of 12 years,[2] but the gradual accumulation of knowledge on the subject brought with it a realization that various degrees of severity of the condition existed,[3] ranging from the mild and asymptomatic to the severe and fatal. A "minor" and a "major" [4] form of the disease were therefore recognized, and it was further demonstrated that the "minor" form was much more prevalent than the more familiar, severe, form.[5] Persons with the "minor" form of the malady were shown to constitute the reservoir of genetic carriers who perpetuated the serious form of the disease,[6] and the term "trait" became synonymous with the "minor" disease. Valentine and Neel [7] have postulated that the defect in the red blood cell is inherited as a mendelian recessive, the condition in heterozygous carriers being manifested as thalassemia minor and in the homozygous carriers as thalassemia major. Because the earlier-discovered instances of this disease occurred almost exclusively in persons of Greek, Syrian, Armenian or South Italian (Sicily, Sardinia, Calabria) extraction, the name Mediterranean anemia and thalassemia ("anemia of the sea") were applied to it, and the racial [2] and familial factor came to be accepted as a part of the clinical syndrome. However, typical cases of Mediterranean anemia have since been reported as occurring in persons of Chinese, Indian, Egyptian, German and Spanish ancestry.[8]

The first reference to the occurrence of typical Mediterranean anemia in a Negro child was made by Dameshek in 1943.[2] The patient was under observation at the Mount Sinai Hospital of New York and showed all the various blood and bone changes characteristic of the disease with consistent absence of sickle cells on blood examination. Faber and Roth in 1946 [9] described an instance of the disease occurring in a 6 year old Negro girl, and Stiles, Manlove and Dangerfield [10] in the same year reported a case of Mediterranean anemia in a 33 year old Negro. More recently, Schwartz and Mason [11] described four cases of Mediterranean anemia occurring in Negro adults and found the disease to be similar in all respects to that found in people of Mediterranean ancestry. The occasional occurrence of thalassemia in Negroes and of sickle cell anemia in Italians and Sicilians [12] is particularly interesting because of genetic and morphological similarities. For instance, sickle cell trait represents heterozygosity and sickle cell anemia homozygosity of the red blood cell abnormality manifested in the sickling defect.[13] The blood smears from persons with thalassemia and sickle cell anemia show consistently more target cells than any other blood dyscrasia.

It may be that the terms Mediterranean anemia and thalassemia are unfortunate ones because they tend to

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Dr. Janet Watson assisted us by reviewing the paper.

From the Medical Service, Veterans Administration Hospital.

Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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focus the search for instances of this disease only on the descendants of the inhabitants of the Mediterranean basin, and Downey [14] may be correct in his feeling that many cases in other races may have been overlooked because of this.

We are reporting the following case of thalassemia minor occurring in an American Negro to add to the small list of previously described cases.

### REPORT OF CASE

A veteran, a 36 year old Negro man, was admitted to the Northport Veterans Administration Hospital on Aug. 23, 1943 by transfer from an Army General Hospital. He had been inducted into the Army in August 1942 and had been sent overseas to the Southwest Pacific Theater in January 1943. In April 1943 he manifested delusions of persecution and auditory hallucinations and was admitted to a station hospital in the New Hebrides Islands, where a diagnosis of a schizophrenic reaction, paranoid type, was made, and he was evacuated to the United States.

The history obtained from available records showed that he was born in San Antonio, Texas, in 1914 and that he was an only child. His father had died while the patient was an infant, and his mother had died of "heart disease" at the age of 42. Physical examination on admission was essentially noncontributory, and he has been continually institutionalized since then. On Aug. 6, 1943 the red blood cell count was 4,560,000, with a hemoglobin content of 88 per cent, and the white blood cell count 8,400, with 64 per cent neutrophils, 34 per cent lymphocytes, 1 per cent monocytes and 1 per cent eosinophils. No malarial parasites were seen in the blood smear, and the Wassermann and Kahn reactions were negative. Spinal fluid and urine were normal.

On Sept. 12, 1944 the red blood cell count was 4,970,000, with a hemoglobin content of 90 per cent. Many stippled red blood cells were noted at this time. The white blood cells included 59 per cent neutrophils, 35 per cent lymphocytes, 3 per cent monocytes, 2 per cent eosinophils and 1 per cent basophils. Blood studies on September 21 again showed numerous stippled red cells, with a red cell count of 5,310,000, a hemoglobin content of 100 per cent, 64 per cent neutrophils, 29 per cent lymphocytes, 4 per cent monocytes, 2 per cent eosinophils, and 1 per cent basophils.

On March 6, 1950 an acute nasopharyngitis developed with a temperature of 100.4 F., and the patient was sent to the medical service for treatment. Physical examination at this time showed a rather light-skinned Negro actively hallucinating. The ocular fundi were normal, and the pupils reacted to light and in accommodation. Acute nasopharyngitis was present. The lungs were clear on percussion and auscultation, and the heart showed a soft systolic murmur of grade II intensity over the aortic area. The blood pressure was 112/70. The liver and spleen were not palpable, but a few small and shotty lymph nodes were present in the right groin. There was a pitting edema (2 plus) of the dorsa of the feet. Rectal examination was noncontributory. Studies of the peripheral blood at this time showed 5,500,000 red cells, a hemoglobin content of 93 per cent and 16,500 white cells, with 66 per cent neutrophils, 29 per cent lymphocytes, 3 per cent monocytes and 1 per cent eosinophils. The reticulocyte count was 1.4 per cent. The red blood cells on smear showed anisocytosis, poikilocytosis and polychromasia. Many red blood cells showed basophilic stippling, and 30 per cent were target cells. The hematocrit reading was 37 per cent, color index 0.84, volume index 0.773, mean corpuscular volume 67.27 cubic microns, mean corpuscular hemoglobin 24.54 micromicrograms and mean corpuscular hemoglobin concentration 36.48 per cent. A red blood cell fragility test showed hemolysis to begin at 0.4 per cent in the control cells and to be complete at 0.28 per cent, while the patient's cells began to show hemolysis at 0.4 per cent dilution and to be completely hemolyzed at 0.04 per cent. Tests for sickling, both direct and latent, gave negative results. Sternal marrow aspiration showed a hyperplastic erythropoiesis of the normoblastic type and red blood cells with basophilic stippling. Many target cells were demonstrable, and anisocytosis, poikilocytosis and polychromasia were marked. Urinalysis was noncontributory, and repeated urobilinogen tests gave negative results in significant dilutions. Blood chemistry studies showed total protein 7.06 Gm. (albumin 4.28 Gm. and globulin 2.78 Gm.); albumin:globulin ratio 1.54; cephalin-cholesterol flocculation, negative; icterus index 8; direct van den Bergh test, negative; indirect test, 0.42 units; cholesterol, 347 mg. per 100 cc., with 73 per cent cholesterol esters; alkaline phosphatase, 8.82 Bodansky units; calcium, 8.87 mg. per 100 cc., and phosphorus, 3.76 mg. per 100 cc. A 24 hour urine specimen did not contain lead. Roentgen studies of the skull, spine and long bones were noncontributory. The stools gave a negative reaction for occult blood. The patient's nasopharyngitis rapidly subsided and the edema of the feet disappeared the morning following admission. This edema was no doubt due to the fact that the patient, because of his mental condition, stood on his feet in one position for long periods, and the edema was of postural origin.

### SUMMARY

A case of thalassemia minor in a Negro is presented. This is the eighth report of its occurrence in Negroes.

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## ADENOSINETRIPHOSPHATE

### TRIAL IN THE TREATMENT OF RHEUMATOID ARTHRITIS

*Lincoln Godfrey, M.D., Philadelphia*

The remarkable results that Hench and his colleagues [1] and subsequently others have obtained in rheumatoid arthritis using cortisone and pituitary adrenocorticotropic hormone (ACTH) have led to the search for other compounds which are more readily available and could produce comparable results. Carlström and Lövgren [2] reported good results in rheumatoid arthritis with the administration of adenosinetriphosphate. Favorable responses occurred within five to 10 days after therapy was begun in the majority of their patients. This rapidity of response with adenosinetriphosphate, in comparison with the slow response of patients treated with gold compounds or other conventional methods, suggested that adenosinetriphosphate influenced the disease in a manner comparable to that of cortisone and pituitary adrenocorticotropic hormone.

Adenosinetriphosphate is a high energy phosphate compound occurring naturally in the body, of great importance in the intermediary metabolism of dextrose. There have been a few scattered reports in the literature of its use in vascular disorders. I have found no reports of toxic reactions.

Twelve patients with severe rheumatoid arthritis were treated with adenosinetriphosphate for varying periods, from five to 11 days. The patients were selected for therapy on the basis of clinical severity and rapid progression of the disease. Only one patient was in the early stage of the disease; the remainder had had rheumatoid arthritis for one or more years. All were having clinical relapses at the time of treat-

From the Medical Clinic, Hospital of the University of Pennsylvania.

1. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: Proc. Staff Meet., Mayo Clin. 24: 181-197 (April 13) 1949.

2. Carlström B., and Lövgren, O.: Acta med. Scandinav. 115: 568-566, 1943.

ment with adenosinetriphosphate, and all needed rather large quantities of both salicylates and codeine for pain relief. The patients were hospitalized during the period of this treatment. Adenosinetriphosphate was administered intramuscularly, 20 mg. dissolved in 2 cc. of isotonic sodium chloride solution every six hours, making a total of 80 mg. every 24 hours. No local or systemic reactions were encountered.

Of the 12 patients treated, 11 failed to show any symptomatic response. Moreover, there was no decrease in joint swelling or increase in range of motion. Four of the 11 patients were treated for 11 consecutive days and six for five consecutive days. One patient, treated for seven days, seemed improved symptomatically and demonstrated some increase in range of motion. Total eosinophil cell counts [3] were done on eight of the 12 patients in an attempt to demonstrate adrenal cortex stimulation. However, there was no significant fall in the total number four hours after the first injection of adenosinetriphosphate, as compared with that immediately prior to administration of the compound. The number of eosinophils in the one patient with symptomatic improvement also failed to show a change. Sedimentation rates were not significantly altered in any patient.

SUMMARY

Eleven of 12 patients with rheumatoid arthritis treated with adenosinetriphosphate failed to show any subjective or objective signs of improvement. These results do not confirm the report by Carlström and Lövgren of the beneficial effect of adenosinetriphosphate in rheumatoid arthritis.

255 South Seventeenth Street.

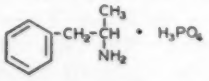
# COUNCIL ON PHARMACY AND CHEMISTRY

## NEW AND NONOFFICIAL REMEDIES

*The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.*

R. T. STORMONT, M.D., *Secretary.*

**Amphetamine Phosphate.** — $C_9H_{13}N.H_3PO_4$.—M.W. 233.21. — Raphetamine Phosphate (Strasenburgh). — Mono-1-phenyl-2-aminopropane phosphate.—The structural formula of amphetamine phosphate may be represented as follows:



*Actions and Uses.*—Amphetamine phosphate shares the actions and uses of amphetamine sulfate. Its one advantage, greater solubility, is significant only in the preparation of solutions for injection. For the indications for its use see the monograph on Amphetamine Sulfate.

*Dosage.*—Doses of amphetamine phosphate approximately 20 per cent greater by weight than those recommended for amphetamine sulfate provide the same amount of the base. Because the average oral dose seldom exceeds 10 mg., the difference between the prescribed amount of the phosphate and sulfate is likely to be clinically undetectable. Theoretically, 12 mg. of amphetamine phosphate represents the approximate equivalent of 10 mg. of amphetamine sulfate. As an analeptic, the drug is administered intravenously or intramuscularly in doses of 20 to 50 mg. every 30 to 60 minutes until consciousness is restored. The same precautions and contraindications must be observed as in the case of other sympathomimetic amine compounds.

*Tests and Standards.*—

*Physical Properties:* Amphetamine phosphate is a white, odorless powder with a bitter taste. It sinters at about 150 C., it becomes an amorphous mass as heating is continued and decomposes at about 300 C. It is freely soluble in water; slightly soluble in alcohol; and practically insoluble in benzene, chloroform and ether. The *pH* of a 10 per cent solution is about 4.6.

*Identity Tests:* Dissolve about 0.1 Gm. of amphetamine phosphate in 5 ml. of water and add a few drops of silver nitrate T.S.: a yellow precipitate forms which is soluble in diluted nitric acid or in ammonia T.S. *(presence of phosphate).*

Dissolve about 0.1 Gm. of amphetamine phosphate in 5 ml. of water and add a few drops of ammonium molybdate T.S.: a yellow precipitate forms which is soluble in ammonia T.S. *(presence of phosphate).*

Place about 1 Gm. of amphetamine phosphate in an Erlenmeyer flask, and add 50 ml. of water and 5 ml. of 40 per cent sodium hydroxide. Then add 5 ml. portions of benzoyl chloride, shaking the flask after each addition, until no more precipitate forms. Recrystallize the benzoyl derivative twice from 50 per cent alcohol and dry the crystals in a vacuum at room temperature for 24 hours: they melt between 134 and 135 C.

*Purity Tests:* Dissolve about 0.5 Gm. of amphetamine phosphate in 50 ml. of water and acidify with hydrochloric acid: separate portions of 10 ml. each of the solution yield no turbidity with 1 ml. of barium chloride T.S. *(absence of sulfate);* and no color or precipitate on saturation with hydrogen sulfide *(absence of salts of heavy metals).*

Dry about 0.5 Gm. of amphetamine phosphate, accurately weighed, to constant weight at 105 C.: the loss in weight is not more than 1 per cent.

Ash about 1 Gm. of amphetamine phosphate, accurately weighed: the residue is less than 0.05 per cent.

*Assay:* (Amphetamine) Dissolve about 0.2 Gm. of amphetamine phosphate, accurately weighed, in 25 ml. of water in a separatory funnel. Add 4 ml. of 10 per cent sodium hydroxide and extract the solution with six 15 ml. portions of chloroform. Wash the combined chloroform extracts with 25 ml. of water. Shake the wash water with an additional 15 ml. of chloroform and add the chloroform layer to the original chloroform extracts. Transfer the chloroform to a glass-stoppered Erlenmeyer flask and shake it with exactly 20 ml. of 0.1 *N* sulfuric acid. Evaporate the chloroform on a steam bath. Cool the solution, add 1 drop of methyl red T.S., and titrate the excess acid with 0.1 *N* sodium hydroxide. Each ml. of 0.1 *N* sulfuric acid consumed is equivalent to 0.01352 Gm. of amphetamine. The amount of amphetamine present is not less than 57.1 nor more than 58.8 per cent, equivalent to not less than 98.5 nor more than 101.5 per cent of amphetamine phosphate.

**Dosage Forms of Amphetamine Phosphate**

SOLUTION. *Assay:* Pipet a volume of solution equivalent to about 0.2 Gm. of amphetamine phosphate into a separatory funnel and proceed as directed in the assay for amphetamine in the monograph for Amphetamine Phosphate. The amount of amphetamine present is not less than 55.1 nor more than 60.9 per cent, equivalent to not less than 95 nor more than 105 per cent of the labeled amount of amphetamine phosphate.

TABLETS. *Assay:* Grind 50 tablets and accurately weigh an amount of powder equivalent to 0.2 Gm. of amphetamine phosphate. Transfer the sample to a glass-stoppered Erlenmeyer flask, add 150 ml. of water and shake the flask for 1 hour. Filter the solution into a 250 ml. volumetric flask, wash the precipitate with five 20 ml. portions of water, and make up to the mark with additional water. Pipet 50 ml. of the solution into a separatory funnel, add 3 ml. of 10 per cent sodium hydroxide, shake and extract the solution with six 20 ml. portions of chloroform. Combine the chloroform extracts in a separatory funnel and wash them with 25 ml. of water. Shake the wash water with an additional 15 ml. of chloroform and add it to the original chloroform extracts. Transfer the chloroform to a glass-stoppered flask and shake it with 50 ml. of 0.02 *N* sulfuric acid. Evaporate the chloroform on a steam bath, cool the solution, add 1 drop of methyl red T.S. and titrate the excess acid with 0.02 *N* sodium hydroxide. Each ml. of 0.02 *N* sulfuric acid consumed is equivalent to 0.002704 Gm. of amphetamine. The amount of amphetamine present is not less than 55.1 nor more than 60.9 per cent, equivalent to not less than 95 nor more than 105 per cent of the labeled amount of amphetamine phosphate.

*Solution Raphetamine Phosphate 1%:* A solution containing 10 mg. of racemic amphetamine phosphate in each cc. Preserved with 0.5 per cent chlorobutanol. R. J. Strasenburgh Co., Rochester, N. Y.

*Tablets Raphetamine Phosphate:* 5 mg. R. J. Strasenburgh Co., Rochester, N. Y.

3. Thorn, G. W.; Forsham, P. H.; Prunty, F. T. G., and Hills, A. G.: J. A. M. A. **137**: 1005-1009 (July 17) 1948.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
535 N. DEARBORN ST. . . . . CHICAGO 10, ILL.
*Edited by* . . . . . AUSTIN SMITH, M.D.
*Associate Editor* . . . . . JOHNSON F. HAMMOND, M.D.
*Editor for Medical Literature Abstracts* . GEORGE HALPERIN, M.D.

Subscription price . . Fifteen dollars per annum in advance
Cable Address . . . . . "Medic, Chicago"

## CHRONIC DISEASE CONFERENCE

"The basic approach to chronic disease must be preventive. Otherwise, the problems created by the chronic diseases will grow larger with time, and the hope of any substantial decline in their incidence and severity will be postponed many years." [1] Acting on this statement of its four founding organizations, the Commission on Chronic Illness has called a three day national Conference on Chronic Disease: Preventive Aspects, to be held March 12-14, 1951, at the Edgewater Beach Hotel in Chicago.

One of the significant contributions planned for the Conference is the preparation of authoritative summaries of existing scientific knowledge applicable to prevention and early detection of the following chronic disease groups [2]: malignant neoplasms; cardiovascular disease; arthritis and rheumatism; neuromuscular disorders, including poliomyelitis, multiple sclerosis, cerebral palsy and epilepsy; diabetes; blindness; deafness; tuberculosis, and syphilis. Summary statements are also planned on the following subjects: emotional factors in chronic disease; malnutrition, including obesity, as a cause of chronic disease; occupational causes of chronic disease, and heredity in chronic disease. These statements are being prepared in advance of the Conference and will be used as a basis for discussion by an expected 150 delegates, who will attempt to determine whether this existing knowledge can be put to wider use to check the growing incidence of chronic disease and what additional research may be needed to increase existing knowledge. Each of the 11 working committees of conferees will discuss a specific channel through which prevention and early detection of chronic disease might be furthered: evaluation of scientific data; application in medical practice; professional information and training for physicians, dentists, nurses, social workers, teachers and health educators; community organization and services, and public information.

Organizations now at work on the statements include the United States Public Health Service and the National Institutes of Health, the American Academy for Cerebral Palsy, American Association of Industrial Physicians and Surgeons, American Cancer Society, American Conference of Governmental Hygienists, American Diabetes Association, American Hearing Society, American Heart Association, American Industrial Hygiene Association, American Psychiatric Association, American Social Hygiene Association, Arthritis and Rheumatism Foundation, Council on Industrial Health of the American Medical Association, Industrial Hygiene Section of the American Public Health Association, National Foundation for Infantile Paralysis, National Multiple Sclerosis Society, National Society for the Prevention of Blindness and the National Tuberculosis Association. Other organizations that have been invited to participate in the preparation of the statements include the American Chapter of the International League Against Epilepsy, Council on Foods and Nutrition of the American Medical Association and the Section on Food and Nutrition of the American Public Health Association.

The expected 150 delegates to the Conference will represent voluntary and official agencies, professional organizations and individuals working in the fields of medicine, hospitals, health, welfare, nursing, dentistry, journalism, education, social work, research and others related to the problems of chronic illness. The Conference should result in focusing national attention on prevention and early detection as the basic long range approach to the chronic disease problem, emphasize the common denominators in the problems that must be overcome in the prevention and early detection of each major chronic disease and accentuate the role of the practicing physician, working with all community agencies, in furthering the prevention of chronic disease and illness.

1. Planning for the Chronically Ill: Joint Statement of Recommendations by the American Hospital Association, American Public Welfare Association, American Public Health Association, and the American Medical Association, which founded the Commission on Chronic Illness in May 1949 to study the problem, J. A. M. A. **135**: 343 (Oct. 11) 1947.

2. Other important diseases and factors related to long term illness have not been included in order to keep the data presented to the Conference within practicable working limits. The question of preparation of additional summary material regarding chronic disease will be considered by all the working committees of the Conference.

## ANTIHISTAMINIC DRUGS IN ACUTE RESPIRATORY DISEASES

It has been postulated that early treatment with antihistaminic drugs reduces complications and prevents dissemination of infectious agents in acute respiratory diseases. A recent study, in which the psychological element was minimized as far as possible by the use of a placebo, showed no evidence that the antihistaminic drug prevented or effected any important alteration in the course of any of several acute respiratory diseases.[1] The study covered Navy male recruits during two influenza episodes. Two antihistaminic drugs were used in therapeutic dosage. These did not prevent the common cold or modify the course in those who developed colds.[2] The use of therapeutic doses before the onset of symptoms did not "abort" colds or effect any important alteration in their symptoms or duration. In another study [3] no evidence was obtained that either atropine or the antihistamine was

1. Prophylaxis and Treatment of Acute Respiratory Diseases with Antihistaminic Drugs: I. Prophylactic Treatment in Navy Male Recruits, J. Lab. & Clin. Med. **36**: 555, 1950.

2. Prophylaxis and Treatment of Acute Respiratory Diseases with Antihistaminic Drugs: II. Prophylactic Treatment with Therapeutic Dosage in Navy Male Recruits, J. Lab. & Clin. Med. **36**: 570, 1950.

3. Prophylaxis and Treatment of Acute Respiratory Diseases with Antihistaminic Drugs: III. Treatment of Minor Acute Respiratory Infection in Navy Wave Recruits, J. Lab. & Clin. Med. **36**: 576, 1950.

effective in aborting or significantly altering the duration of symptoms. Similar effects on the nasal mucosa and secretion were observed with both drugs. The antihistaminic drug had an atropine-like effect on the nasal mucosa. Thus the appearance of the nasal mucosa as a criterion for "cure" in the evaluation of these drugs against colds may prove misleading, as the appearance of the nasal mucosa after antihistamine therapy is related to the atropine-like and not the antihistaminic effect of these drugs. The results of a study of a population with extensive contacts with surrounding communities, and in which the "colds" would be representative of those prevalent in civil populations, disclosed a high degree of psychological benefit derived from the placebos, and the antihistamines showed no superiority over them.[4] Results of this study are not in agreement with those of some studies, in which beneficial results were purportedly obtained, and it points out the fallacies of some of these deductions. In spite of the many claims that have been made for the usefulness of antihistamines for colds, there is not yet any preponderance of evidence that these drugs can provide more than symptomatic relief.

## THE EASTER SEAL CAMPAIGN

Americans are friendly, independent and aggressive people, who like to face their responsibilities squarely and do their best to meet them fully. One of these responsibilities, as they see it, is helping others less fortunate than themselves. Americans have shown repeatedly that they like to help their neighbors in distress, not waiting for the services of government to do a job they feel they can do better themselves.

An outstanding example of this is the help Americans today are giving the nation's crippled children. In several brief decades, the prospect of useful living has been changed for the millions of youngsters in the United States who bear handicaps of various kinds. This change has come about because Americans were not content to see children relegated to back bedrooms or confined to wheel chairs if there was a single hope of bettering their condition. Science in the United States has made tremendous strides in the medical, surgical and therapeutic treatment of crippled children.

Because it was not content, the American public rolled up its sleeves and went to work to organize, to finance and keep expanding a great nationwide effort to help crippled children—a typically and essentially American way of promoting public interest in the health and welfare of these children.

The National Society for Crippled Children and Adults, which with its state and local affiliates makes available to thousands of crippled children the latest advances of science and its related fields, is the form this voluntary effort has taken. The services and facilities of this federation of societies, made possible by the contributions of millions of Americans to the annual Easter Seal drive, have helped thousands of children walk, talk and live as vital members of their families, their communities and their nation. Surely no cause can be more impelling in its appeal than one that means so much to so many children and to the future of a nation. It is a privilege for every one to be able to give voluntarily to the Easter Seal campaign between February 25 and March 25, 1951, and at the same time lend strength to a great democratic cause expressing the human impulse to help others.

## FOOD ACIDS AND CARIES

The concept that acid erosion is the fundamental cause of dental caries was advanced more than half a century ago. Further experimental evidence supporting this hypothesis was recently presented. From a microbiologic point of view, the demonstration [1] of the high acidophilus count in carious mouths was of great significance, since it revealed a mechanism for the production of acid food residues. Another important observation was that in a group of children the only significant difference between the composition of the saliva of caries-free and of carious mouths was the strikingly higher buffer capacity of the former.[2] In line with this finding was the demonstration [3] that removal of the salivary glands in rats resulted in severe hypertrophic gingivitis and caries on the exposed surfaces of the molars in less than three weeks.

Improved technics for experimental study of caries have been introduced recently. The Syrian hamster has been used widely as an experimental animal, since it was shown to have a tooth structure more like that of human teeth than that of other rodents.[4] Ordinarily the common laboratory albino rat is not readily susceptible to caries, the cotton rat being more useful in studies of this disease.[5] However, if the mothers of young albino rats are restricted to purified caries-producing rations during pregnancy and lactation, their progeny become as susceptible to tooth decay [6] as the cotton rat. That contact of food with the tooth surface is a prerequisite for caries production seems clear from an investigation [7] in which a caries-producing ration was fed to young rats through a stomach tube. While lesions developed in all of the control group eating the diet, the rats receiving the food through the tube were not affected.

"Soft" drinks, which usually contain a considerable concentration of organic acid in addition to flavoring, sugar and carbon dioxide, and acid-sugar combinations that simulate "soft" drinks, produce etching of the enamel and dentine of the teeth of laboratory rats, hamsters and dogs.[8] Apparently the acid attack is a function of the titratable acidity of the beverage rather than the $p_H$, while the buffering action of the saliva [9] serves

4. Prophylaxis and Treatment of Acute Respiratory Diseases with Antihistaminic Drugs: IV. Prophylaxis and Treatment of "Colds" in Volunteers, J. Lab. & Clin. Med. **36**: 584, 1950.

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2. Hubbell, R. B.: Am. J. Physiol. **105**: 436, 1933.
3. Weisberger, D.; Nelson, C. T., and Boyle, P. E.: Am. J. Orthodontics **26**: 88, 1940.
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5. Shaw, J. H.; Schweigert, B. S.; McIntire, J. M.; Elvehjem, C. A., and Phillips, P. H.: J. Nutrition **28**: 333, 1944.
6. Sognnaes, R. F.: J. Nutrition **36**: 1, 1948.
7. Kite, O. W.; Shaw, J. H., and Sognnaes, R. F.: J. Nutrition **42**: 89, 1950.
8. McClure, F. J.: J. Nutrition **26**: 251, 1943. Bieri, J. G.; McCay, C. M.; Restarski, J. S., and Gortner, R. A., Jr.: Arch. Biochem. **11**: 33, 1946.

to oppose the erosive action. Acid fruit juices have been recently implicated, and the citrate ion seems particularly prone to produce dental lesions. In one study,[10] apple, grape, pineapple, orange and grapefruit juices produced pronounced erosion of the lower molars in the albino rat while tomato and prune juices had a much milder action. A recent investigation [11] of Polynesian fruits—grapefruit, guava, Java plum, mango and pineapple—confirmed the erosive action of acid fruit juices on dental enamel, but when an equivalent amount of the fruit itself was consumed there was much less etching of the tooth substance.

The role of nutrition in the etiology of dental caries has received considerable attention, and vitamins and minerals have been regarded as factors specially involved in dental health. Although there are doubtless nutritional and metabolic factors favoring the development and integrity of the teeth, the presence of acidity, either preformed in food touching the surface of the teeth or developed by bacterial degradation of food residues in the crevices around the teeth, appears to be a prominent factor in the erosion of the enamel and dentine.

## NEUROMUSCULAR BLOCKING BY DRUGS

Skeletal muscle relaxants are commonly employed as adjuncts in general anesthesia and shock therapy and in the treatment of various spastic conditions. Most widely used to date have been curare and its derivatives, including the purified principle *d*-tubocurarine. Recently, several synthetic agents, such as mephenesin (myanesin) decamethonium and flaxedil® (1,2,3-tri[diethylaminoethoxy]benzene triethyliodide) have been introduced, the last two having had more extensive clinical trial in Great Britain than in this country. In a recent article, Paton and Zaimis [1] draw attention to the fundamental differences in action between *d*-tubocurarine and decamethonium and discuss the significance of these differences in the clinical assessment of these drugs and related compounds.

Paton and Zaimis point out that muscles vary in their sensitivity to *d*-tubocurarine and to decamethonium but the differences are not the same with the two drugs. Thus in the cat, the respiratory muscles are paralyzed before the tibialis with *d*-tubocurarine and after the tibialis with decamethonium. Furthermore, there are species variations in sensitivity to the two drugs; the rat, for example, is particularly sensitive to *d*-tubocurarine but relatively insensitive to decamethonium, while in the cat the reverse relation obtains. Ether anesthesia slightly potentiates *d*-tubocurarine but slightly antagonizes decamethonium. Injection of epinephrine serves to increase the initial stimulant action of decamethonium, changes the potency of *d*-tubocurarine and of decamethonium on a given muscle and changes the pattern of muscle susceptibility to these two drugs in opposite ways. It can be readily appreciated that tests of these compounds on unanesthetized subjects will be seriously influenced by the endogenous secretion of epinephrine which such trials must provoke, and the results observed may therefore be irrelevant to those obtained under conditions of surgical anesthesia.

Paton and Zaimis believe that the differences between *d*-tubocurarine and decamethonium are due to the fact that these two drugs effect neuromuscular blockade by fundamentally different mechanisms. Transmission of impulses from motor nerves to voluntary muscle was shown by Dale in 1936 to involve liberation of acetylcholine at the end plates. It is thought that the acetylcholine depolarizes the muscle membrane at the end plate, causing a brief excitation, while immediate hydrolysis of the acetylcholine by cholinesterase permits repolarization so that a second impulse can again result in depolarization and excitation. Decamethonium also depolarizes the muscle membrane, but with this drug depolarization is presistent, so that after a brief initial stimulation neuromuscular block occurs. *d*-Tubocurarine, on the other hand, does not depolarize the muscle but exerts its action simply by raising the threshold of the motor end plate to acetylcholine. Thus it is not surprising that anticholinesterases should antagonize *d*-tubocurarine but not decamethonium.

Seriously misleading results may be obtained if the differences between the drugs are not borne in mind, and, as the authors point out, "a comparison of the clinical usefulness of such drugs as *d*-tubocurarine and decamethonium can only be made under the conditions of actual use." Such clinical trials may also reveal differences between the drugs that may be, in time, capable of exploitation in other directions and yield further information relative to the physiology of the human neuromuscular junction.

## LOCAL PUBLIC HEALTH UNITS

The Committee on Legislation of the American Medical Association met jointly with the Executive Committee of the Board of Trustees on January 22 in Washington, D. C., and considered pending legislation. The Priest Bill, H.R. 274, which amends the Public Health Service Act to authorize assistance to the states and political subdivisions in the development and maintenance of local public health units, particularly in national defense areas, received particular consideration. The president of the Association of State and Territorial Health Officers, Dr. Roy L. Cleere, met with the committees of the American Medical Association to discuss this bill. Congressman Priest also discussed the bill and indicated his favorable reactions to several changes that were suggested. After careful consideration of all aspects of this legislation, the Committee on Legislation and the Executive Committee of the Board of Trustees unanimously approved H.R. 274 and other similar health units bills now pending, with the understanding that amendments will be made to enhance local autonomy and clarify the types of service that may be rendered.

9. Miller, R. F., and Gortner, R. A., Jr.: Arch. Biochem. **20**: 153, 1949.
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11. Miller, C. D.: J. Nutrition **41**: 63, 1950.
1. Paton, W. D. N., and Zaimis, E. J.: Actions and Clinical Assessment of Drugs Which Produce Neuromuscular Block, Lancet **2**: 568, 1950.

# ORGANIZATION SECTION

## THE PHYSICIAN'S FEDERAL INCOME TAX

Federal income taxpayers on a calendar year basis must on or before March 15 do two things: 1. They must file their final returns for the year 1950. 2. They must file a declaration of estimated tax for 1951.

Normal and surtax rates applicable to 1950 income were not changed by the Revenue Act of 1950. The net effect of the provisions of that act, however, will be that taxpayers will be required to pay a higher tax than was required the previous year. This result follows the reduction of the percentage amount by which the tentative tax may be reduced. That amount is about one-fourth less than it was prior to the enactment of the new act.

Copies of appropriate forms have already been distributed to prior taxpayers, together with a small booklet which presents the general requirements of the law. Physicians who are for the first time subject to the requirements of the federal income tax law may obtain the necessary forms from the office of the Collector of Internal Revenue having jurisdiction.

### GROSS INCOME

A physician's gross income is the total amount of money received by him during the year for professional services, regardless of the time when the services were rendered for which the money was paid, assuming that the return is on a cash receipts and disbursements basis, plus such money as he has received from investments and from other sources.

If a physician receives a salary as compensation for services rendered and in addition thereto living quarters or meals, the value to the physician of the quarters and meals so furnished ordinarily constitutes income subject to tax. If, however, living quarters or meals are furnished for the convenience of the employer, the value thereof need not be computed and added to the compensation otherwise received by the physician unless such quarters and meals are furnished as a part of compensation.

### DEDUCTIONS FOR PROFESSIONAL EXPENSES

A physician is entitled to deduct all current expenses necessary in carrying on his practice. The taxpayer should make no claim for the deduction of expenses unless he is prepared to prove the expenditure by competent evidence. As far as practicable, accurate itemized records should be kept of expenses and substantiating evidence should be carefully preserved. The following statement shows what such deductible expenses are and how they are to be computed:

*Office Rent.*—Office rent is deductible. If a physician rents an office for professional purposes alone, the entire rent may be deducted. If he rents a building or apartment for use as a residence as well as for office purposes, he may deduct a part of the rental fairly proportionate to the amount of space used for professional purposes. If the physician occasionally sees a patient in such dwelling house or apartment, he may not, however, deduct any part of the rent of such house or apartment as professional expense; to entitle him to such a deduction he must have an office there, with regular office hours. If a physician owns the building in which his office is located, he cannot charge himself with "rent" and deduct the amount so charged.

*Office Maintenance.*—Expenditures for office maintenance, as for heating, lighting, telephone service and the services of attendants, are deductible.

*Supplies.*—Payments for supplies for professional use are deductible. Supplies may be fairly described as articles consumed in the using; for instance, dressings, clinical thermometers, drugs and chemicals. Professional journals may be classified as supplies and the subscription price deducted. Amounts currently expended for books, furniture and professional instruments and equipment, "the useful life of which is short," generally less than one year, may be deducted, but if such articles have a more or less permanent value, their purchase price is a capital expenditure and is not deductible.

*Equipment.*—Equipment comprises property of a more or less permanent nature. It may ultimately wear out, deteriorate or become obsolete, but it is not in the ordinary sense of the word "consumed in the using."

The cost of equipment such as has been described, for professional use, cannot be deducted as expense in the year acquired. Examples of this class of property are automobiles, office furniture, medical, surgical and laboratory equipment of more or less permanent nature, and instruments and appliances constituting a part of the physician's professional outfit, to be used over a considerable period of time, generally over one year. Books of more or less permanent nature are regarded as equipment, and the purchase price is therefore not deductible.

Although the cost of such equipment is not deductible in the year acquired, nevertheless it may be recovered through depreciation deductions taken year by year over its useful life, as described later.

No hard and fast rule can be laid down as to what part of the cost of equipment is deductible each year as depreciation. The amount depends to some extent on the nature of the property and on the extent and character of its use. The length of its useful life should be the primary consideration. The most that can be done is to suggest certain average or normal rates of depreciation for each of several classes of articles and to leave to the taxpayer the modification of the suggested rates as the circumstances of his particular case may dictate. As fair, normal or average rates of depreciation, the following have been suggested: automobiles, 25 per cent a year; ordinary medical libraries, x-ray equipment, physical therapy equipment, electrical sterilizers, surgical instruments and diagnostic apparatus, 10 per cent a year; office furniture, 5 per cent a year.

The principle governing the determination of all rates of depreciation is that the total amount claimed by the taxpayer as depreciation during the life of the article, plus the salvage value of the article at the end of its useful life, shall not be greater than its purchase price. The physician must in good faith use his best judgment and claim only such allowance for depreciation as the facts justify. The estimate of useful life, on which the rate of depreciation is based, should be carefully considered in each case.

*Dues.*—Dues paid to societies of a strictly professional nature are deductible. Dues paid to social organizations, even though their membership is limited to physicians, are generally held to constitute personal expenses and as such are not deductible. If, however, membership in social organizations, such as a country club, is maintained both for personal and professional or business purposes and if evidence can be produced to substantiate the claim that a part of the expenses of such membership was incurred for business purposes, then it would seem that these latter expenses would be deductible. Further discussion of this particular aspect of the federal law will be found in a subsequent paragraph dealing with the deductibility of entertainment expenses.

*Postgraduate Study.*—The Commissioner of Internal Revenue holds that the expense of postgraduate study is not deductible.

*Traveling Expenses.*—Traveling expenses, including amounts paid for transportation, meals and lodging, necessarily incurred in professional visits to patients and in attending medical meetings for a professional purpose, are deductible.

*Entertainment Expenses.*—The deductibility of entertainment expenses, when incurred for business purposes, has been upheld, as applied to an actor, in the case of *Blakmer v. Commissioner*, 70 F. (2d) 255. In the case of *Jacobson*, 6 T.C. 1048, the taxpayer was allowed a deduction of expenses incurred for entertaining clients and employees of his law firm. The deductibility

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Prepared by the Bureau of Legal Medicine and Legislation, American Medical Association.

of such expenses by an attorney came before the U. S. Tax Court in the case of *Clyde A. Armstrong v. Commissioner*, decided Aug. 29, 1947, 6 TCM 997. In a memorandum opinion rendered by Judge Opper, this was said:

> Taxpayer, a Pittsburgh attorney, became a member of the University Club and the Duquesne Club in order to have available facilities for the entertainment of his clients; his purpose in joining the clubs was not particularly to make contacts productive of new business. In 1942, 1943 and 1944 the Commissioner disallowed deductions representing club dues, but allowed 50 per cent of the house bills incurred by taxpayer at each of the clubs during those years. The court finds that taxpayer used the club facilities not less than 50 per cent of the time for entertaining clients and other purposes incident to the practice of his profession, and allows the deduction of dues to that extent.

In the December 1948 issue of the *Medical Annals of the District of Columbia*, page 697, there was published correspondence that had passed between the secretary of the Medical Society of the District of Columbia and the Internal Revenue Agent in the Baltimore Division, Treasury Department, in which the latter stated that if entertainment expenses incurred by a physician have a direct relation to the production of income, and can be supported by the taxpayer, they will be taken into consideration in determining his net taxable income.

*Automobiles.*—Payment for an automobile is a payment for permanent equipment and is not deductible. The cost of operation and repair, and loss through depreciation, are deductible. The cost of operation and repair includes the cost of gasoline, oil, tires, insurance, repairs, garage rental (when the garage is not owned by the physician), chauffeur's wages and the like.

Deductible loss through depreciation of an automobile is the actual diminution in value resulting from obsolescence and use and from accidental injury against which the physician is not insured. If depreciation is computed on the basis of the average loss during a series of years, the series must extend over the entire estimated life of the car, not merely over the period in which the car is possessed by the present taxpayer.

If an automobile is used for professional and also for personal purposes—as when used by the physician partly for recreation, or so used by his family—only so much of the expense as arises out of the use for professional purposes may be deducted. A physician doing an exclusive office practice and using his car merely to go to and from his office cannot deduct depreciation or operating expenses; he is regarded as using his car for his personal convenience and not as a means of gaining a livelihood. What has been said in respect to automobiles applies with equal force to horses and vehicles and the equipment incident to their use.

*Surgical Uniforms.*—Amounts expended by surgeons for the purchase and maintenance of distinctive types of uniforms which are not adaptable to ordinary wear and which are required to be worn while on duty are deductible as ordinary and necessary business expenses.

### MISCELLANEOUS

*Contributions to Charitable Organizations.*—For detailed information with respect to the deductibility of charitable contributions generally, physicians should consult the official return blank or obtain information from the collectors of internal revenue or from other reliable sources. An individual taxpayer can deduct such contributions only to the extent that they do not exceed 15 per cent of his adjusted gross income. The physician may not deduct as a charitable contribution the value of services rendered an organization operated for charitable purposes.

*Bad Debts.*—Physicians who make their returns on a cash receipts and disbursements basis, as most physicians do, cannot claim deductions for bad debts.

*Taxes.*—Taxes generally, either federal or state, are deductible by the person on whom they are imposed by law. Both real and personal property taxes are deductible; but so-called taxes, more properly assessments, paid for local benefits, such as street, sidewalk and other like improvements, imposed because of and measured by some benefit inuring directly to the property against which the assessment is levied, do not constitute an allowable deduction from gross income. Physicians may deduct state gasoline taxes and state sales taxes. In some states sales taxes are imposed on the seller, but if they are passed on to the buyer the latter may deduct them.

State income and use taxes are deductible; federal income taxes are not. Federal import, excise or stamp taxes are deductible only to the extent that they are attributable to business activities. State automobile license fees are deductible. If a state or local fee is imposed for regulatory purposes, and not to raise revenue, the fee may not ordinarily be deducted as a tax. If such fees, however, are classifiable as a business expense they are deductible as such. Annual registration fees imposed on physicians probably come within the category of regulatory fees and should be deducted as a business expense rather than as taxes. Local and state occupational taxes imposed on physicians are deductible either as taxes or as a business expense, depending on the purpose for which the tax is imposed.

The excise taxes imposed on employers by section 804, title VIII, and section 901, title IX, of the Social Security Act, commonly referred to as old age and unemployment benefit taxes, are deductible annually by employers in computing net income for federal income tax purposes. If the taxpayer's return is made on a cash basis, as are the returns of practically all physicians, the taxes are deductible for the year in which they are actually paid. If the return is made on an accrual basis, the taxes are deductible for the year in which they accrue, irrespective of when they are actually paid. Employees, including physicians whose employment brings them within that category, may not deduct the tax imposed on them by section 801, title VIII, of the Social Security Act, generally referred to as the old age benefits tax. If, however, the employer assumes payment of the employee's tax and does not withhold the amount of the tax from the employee's wages, the amount of the tax so assumed may be deducted by the employer, not as a tax paid but as an ordinary business expense.

*Medical Expense.*—A taxpayer may deduct amounts expended for medical, dental and hospital expense for himself, his spouse or a dependent, not compensated for by insurance or otherwise, including amounts paid for health and accident insurance, according to a prescribed formula. The law limits the deduction to a maximum of (*a*) $1,250 if the taxpayer claims only one exemption; (*b*) $2,500 if the taxpayer is a single person or if married and filing a separate return and claims more than one exemption; (*c*) $2,500 if the taxpayers are married and file a joint return and claim two exemptions, $3,750 if three exemptions are claimed and $5,000 if four or more exemptions are claimed.

*Laboratory Expenses.*—The deductibility of the expenses of establishing and maintaining laboratories is determined by the same principles that determine the deductibility of corresponding professional expenses. Laboratory rental and the expenses of laboratory equipment and supplies and of laboratory assistants are deductible when under corresponding circumstances they would be deductible if they related to a physician's office.

*Losses by Fire or Other Causes.*—Loss of and damage to a physician's equipment by fire, theft or other cause, not compensated by insurance or otherwise recoverable, may be computed as a business expense and is deductible, provided evidence of such loss or damage can be produced. Such loss or damage is deductible, however, only to the extent to which it has not been made good by repair and the cost of repair claimed as a deduction.

*Insurance Premiums.*—Premiums paid for insurance against professional losses are deductible. This includes insurance against damages for alleged malpractice, against liability for injuries by a physician's automobile while in use for professional purposes, and against loss from theft of professional equipment and damage to or loss of professional equipment by fire or otherwise. Under professional equipment is to be included any automobile belonging to the physician and used for strictly professional purposes.

*Expense in Defending Malpractice Suits.*—Expense incurred in the defense of a suit for malpractice is deductible as a business expense.

*Sale of Spectacles.*—Oculists who furnish spectacles, etc., may charge as income money received from such sales and deduct as an expense the cost of the article sold.

## HEALTH EXHIBITS

The American Medical Association has available exhibits that are designed for public showing at fairs and expositions. Each exhibit is completely prepared and so designed as to require no background or special accessories. These exhibits are available on a loan basis without cost except transportation charges. Requests for material should be instituted as far in advance as possible, so that the proper reservations can be made. Requests from groups other than medical societies should be made through the secretary of the local county or state medical society or approval of such society obtained. Exact shipping addresses and dates should be given when the request is made.

Responsibility for installation and demonstration of the exhibits ordinarily must be borne by the organization to which the material is loaned. The American Medical Association does not have the personnel for such duties. Expenses include the items incidental to the installation and demonstration of the exhibit, as well as transportation charges both ways. Shipments will be made either by freight or by express, according to request.

Literature for distribution is not sent free with the exhibits but must be purchased from the Order Department of the American Medical Association. The prices quoted are for single copies; for quantity discounts write the Order Department. Further information may be obtained from the Director, Bureau of Exhibits, American Medical Association, 535 North Dearborn Street, Chicago 10.

1. *Your Bones and Muscles.*—Visitors to this exhibit will have an opportunity to participate by manipulating mechanical devices in the three cases that demonstrate (1) the effect of proper and improper posture, (2) the kind of levers that are used in the bone and muscle structure of the body and (3) the several types of bone joints.

The subject matter treated relates to the growth of bones, emphasizing the need of plenty of sunlight, vitamin D from other sources; the structure of the body, showing the skeleton; the structure of the bones, the location and the structure of the muscles of the body. An information file and question box form a part of the exhibit. Space required, an area 10 feet long by 6 feet deep. No booth background is necessary. Electrical connections, three outlets using 300 watts. Shipping weight, about 580 pounds.

Literature available from the American Medical Association Order Department:

"Wonder Stories of the Human Machine"

I. The Framework (Bones), 15 cents

II. The Running Gear (Muscles), 15 cents

2. *The Skin in Health and Disease.*—The focal point of attention in this exhibit is a unique and fascinating visitor participation case showing the effect of heat and cold on the skin. By pressing the button on this center piece, the warming effect of shivering is demonstrated. The cooling effect of perspiration evaporation is also shown.

That the care of the skin is one of the most popular health topics is evidenced by the preponderance of questions on this subject received by *Today's Health* and the Bureau of Health Education of the American Medical Association. Among the phases of the subject emphasized in this exhibit are cosmetics, baldness, superfluous hair, tanning and sunburn, and chapping and frostbite.

Visitors may take their own skin temperatures at another visitor participation unit that comprises part of the exhibit. An information file contains answers to over 30 questions on the care and diseases of the skin. Space required, an area 10 feet wide by 6 feet deep; no background necessary.

Electrical requirements, one connection for mechanical model, about 200 watts. Shipping weight, 360 pounds.

Literature available from the American Medical Association Order Department:

The Skin in Health and Disease, Harold N. Cole, 8 pages, 15 cents

"Wonder Stories of the Human Machine"

The Breather Pipes and Thermostatic Control (Lungs and Skin), 15 cents

The Body Finish, 15 cents

Perspiration, Herman Goodman, 3 pages, 5 cents

"Hair-Brained" Notions, Lois Mattox Miller, 12 pages, 10 cents

Superfluous Hair and Acne, Samuel M. Kaufman, 8 pages, 15 cents

Cosmetic Facts and Fancies, Austin Smith, 8 pages, 15 cents

Psoriasis, the Threadbare Mantle, Lester Hollander, 12 pages, 15 cents

Fire Under the Skin, William W. Bolton, 9 pages, 15 cents

Superfluous Hair and Acne—Cause and Cure, Samuel M. Kaufman, 3 pages, 5 cents

The Care of the Skin, Everett C. Fox, 4 pages, 5 cents

Birthmarks, Joseph Jordan Eller, 2 pages, 5 cents

The Common Wart, R. H. Rulison, 3 pages, 5 cents.

Boil Busters, William W. Bolton, 5 pages, 5 cents

3. *The Respiratory System in Health and Disease.*—A dramatic exhibit in which visitors have several opportunities to participate. The center of attraction is a rubber model of human lungs showing how the lungs expand when the diaphragm is pulled down. The use of the bronchoscope is shown by means of a relief figure that, when transilluminated, demonstrates where the bronchoscope reaches when it is inserted.

The exhibit contains a panel on which is mounted a fascinating variety of foreign bodies, accidentally but commonly inhaled into the lungs. The use of the nasopharyngoscope is demonstrated by a relief figure panel that requires participation by pressing a button to illuminate the area. Several panels contain posters showing the anatomic structure of the lungs, pneumothorax, tuberculosis, silicosis, pneumonia and the common cold.

Space required, an area 10 feet wide by 6 feet deep. No tables or back walls are needed. Electrical requirements, three outlets for lamps totaling about 200 watts. Shipping weight, 479 pounds.

Literature available from the American Medical Association Order Department:

"Wonder Stories of the Human Machine"

III. The Breather Pipes and Thermostatic Control (Lungs and Skin), 15 cents

9. *Dangers of Self Diagnosis and Self Medication.*—The attention of the visitor to this exhibit is directed to the skill that is involved in making an accurate diagnosis and the parallel skill in pursuing the proper treatment. Three visitor participation devices are incorporated as a part of the exhibit. One is a relief figure showing a physician using a gastroscope; the second, a physician using an otoscope, and the third, a demonstration of the use of the sigmoidoscope. Four panels outline the dangers of self diagnosis of tuberculosis, appendicitis, cancer and aches and pains.

Space required, an area 10 feet wide by 10 feet deep (or 16 feet wide by 6 feet deep). No background is necessary. Two tables 3 feet long for information files. Electrical connections, one outlet, 250 watts. Shipping weight, approximately 400 pounds.

10. *The Care of the Heart.*—Heart disease caused by acute rheumatic fever and syphilis are particularly emphasized in this exhibit. The prevalence of heart disease, intelligent care in living with heart disease and the factors that tax the diseased heart are also portrayed in the various charts. An information file containing the answers to 30 common questions about heart disease is available for shipment with this exhibit. This exhibit is presented with the cooperation of the University of Illinois College of Medicine.

Space required, an area 10 feet long by 6 feet deep; no booth background necessary. Electrical requirements, 1,000 watts, either alternating or direct current. Shipping weight about 500 pounds.

Literature available from the American Medical Association Order Department:

Heart Attack, Walter Modell, 12 pages, 15 cents

Healthy Hearts, a collection of *Today's Health* (formerly *Hygeia*) articles on the subject, 20 pages, 15 cents

Varicose Veins, Morris Friedell, 8 pages, 10 cents

High Blood Pressure, Irvine H. Page and A. C. Corcoran, 8 pages, 15 cents

"Wonder Stories of the Human Machine"

IV. The Engine (Heart), 15 cents

11. *The Failing Heart.*—The center of interest in this exhibit is a large transparency case containing a stylized heart that shows the circulation of the blood through the heart. A flasher system is employed to illuminate arrows one after another to trace this circulation. The colored drawings on the panels show the cause of endocarditis and the infections that are most frequently responsible for it. Myocarditis is depicted in a similar way, with emphasis on the infectious diseases most frequently responsible for myocarditis, such as scarlet fever, typhoid, diphtheria and measles. A definition of heart disease is given. Also shown are the conditions responsible for coronary disturbances of the heart.

An information file is provided containing the answers to approximately thirty common questions on heart disease. A question box is available so that visitors may write out questions on heart disease, which will be answered by the Bureau of Health Education of the American Medical Association. This exhibit is presented with the cooperation of the University of Illinois College of Medicine.

Space required, an area 10 or 12 feet long by 6 feet deep; no booth background is necessary. Electrical requirements, alternating current only, approximately 500 watts. Shipping weight, 502 pounds.

Literature available from the American Medical Association Order Department:

Heart Attack, Walter Modell, 12 pages, 15 cents

Healthy Hearts, a collection of *Today's Health* (formerly *Hygeia*) articles on the subject, 20 pages, 15 cents

Varicose Veins, Morris Friedell, 8 pages, 10 cents

High Blood Pressure, Irvine H. Page and A. C. Corcoran, 8 pages, 15 cents

"Wonder Stories of the Human Machine"

IV. The Engine (Heart), 15 cents

12. *The Neglected Heart.*—The end results of a neglected heart are shown in this exhibit through the medium of five dioramas of small figures. A large center diorama shows a patient by an examining table. The physician has just completed a periodic physical examination and the caption of the diorama is "How to Live with Your Heart." Flanking the model figures are two illuminated cases, one case containing a three dimensional plaque showing an actual stethoscope in use, and the second case containing another three dimensional plaque showing the instrument used in measuring blood pressure.

An information file is provided, containing the answers to approximately 30 common questions on heart disease. A question box is available so that visitors may write out questions on heart disease, which will be answered by the Bureau of Health Education of the American Medical Association.

The exhibit is presented with the cooperation of the University of Illinois College of Medicine. Space required, an area 10 feet long by 6 feet deep; no booth background is necessary. Electrical connections, sufficient to provide 500 watts. Shipping weight, 742 pounds.

Literature available from the American Medical Association Order Department:

Heart Attack, Walter Modell, 12 pages, 15 cents

Healthy Hearts, a collection of *Today's Health* (formerly *Hygeia*) articles on the subject, 20 pages, 15 cents

Varicose Veins, Morris Friedell, 8 pages, 10 cents

High Blood Pressure, Irvine H. Page and A. C. Corcoran, 8 pages, 15 cents

"Wonder Stories of the Human Machine"

IV. The Engine (Heart), 15 cents

19. *Maternal and Child Health.*—The exhibit consists of two illuminated cases and four panels. One of the illuminated cases shows the pelvimeter and the other shows a normal and abnormal female pelvis. The panels depict two subjects, the mother and the child. On the panels devoted to the mother, the subjects treated are medical advice, nutrition, exercise and rest. On the panels devoted to the child, the subjects treated are feeding the baby, play, childhood diseases and parental authority. An information file and question box accompany the exhibit. Space required, an area 10 feet wide and 6 feet deep. Electrical connections, one outlet of 250 watts. Shipping weight, about 400 pounds.

Literature available from the American Medical Association Order Department:

Streamlined Motherhood, Marjorie F. Marks, 8 pages, 15 cents

A Child Is to Be Born, a booklet prepared by the American Medical Association for the expectant mother, 45 pages, 15 cents

Keeping Your Baby Well, 22 pages, 10 cents

Bad Habits in Good Babies, Herman M. Jahr, 16 pages, 15 cents

Bladder Control, Herman M. Jahr, 12 pages, 20 cents

The Case of the Crying Baby, Herman M. Jahr, 4 pages, 10 cents

What to Do About Thumb Sucking, William I. Fishbein, 6 pages, 10 cents

Safeguarding the Take-Off to School, Gaylord W. Graves, 8 pages, 10 cents

Protecting Your Child from Allergy, William Gayle Roberts, 8 pages, 10 cents

How to Manage the Adolescent, Smiley Blanton, 4 pages, 10 cents

Tonsils, Frank J. Novak Jr. and Roberta Hill, 8 pages, 10 cents

Pregnancy, Edith Potter, 49 pages, 15 cents

Saving Your Figure, Charlotte R. Welsh, 5 pages, 5 cents

(Write for complete list).

20. *Tuberculosis.*—The center of this exhibit consists of nine transparencies showing roentgenograms of tuberculosis, depicting what happens in a partial collapse of the lung, and emphasizes that through surgical procedures many cases of tuberculosis recover and are rehabilitated. Charts and pictures emphasize how tuberculosis is spread, the means employed in the diagnosis of the disease and the treatment followed. The steps that can be followed in the prevention of tuberculosis are also shown.

The answers to approximately 30 questions concerning tuberculosis are given in the information file accompanying the exhibit. A question box is shipped with the exhibit, where visitors can write any questions on tuberculosis. These questions are answered by the Bureau of Health Education of the American Medical Association.

This exhibit is presented with the cooperation of the University of Illinois College of Medicine. Space required, an area 10 feet long by 6 feet deep. No booth background necessary. Electrical connections, one outlet using 300 watts for transparency case. Shipping weight about 400 pounds.

Literature available from the American Medical Association Order Department:

Tuberculosis, E. A. Thacker, 12 pages, 15 cents

Surgery in Tuberculosis, Louis Carp, 12 pages, 15 cents.

The Use of X-Rays in Diseases of the Chest, J. A. Myers and Virginia L. Dustin, 16 pages, 15 cents

Tuberculosis Organizations, J. A. Myers and Virginia L. Dustin, 28 pages, 20 cents

From Whom Did He Get It? To Whom Has He Given It? J. A. Myers, 16 pages, 10 cents

22. *Cancer.*—The feature attraction in this exhibit is a large figure 7 equipped with a motor that illuminates the seven cancer danger signals in sequence. The panels of pictorial material set forth the early signs of cancer, such as any sore that does not heal, persistent indigestion and bloody discharge. Another panel shows that there are only three ways to treat cancer, namely, surgery, roentgen rays and radium. Early treatment is emphasized by the statement that 70 per cent are alive after five years when the treatment is early, whereas only 4 per cent live five years when the treatment is late.

Two information files give the answers to over 60 questions, such as on heredity, contagiousness and causes.

Space required, an area 10 feet wide by 7 feet deep. No background necessary. Electrical connections, one outlet using about 100 watts. Shipping weight, 400 pounds.

Literature available from the American Medical Association Order Department:

When Cancer Is Not Guilty, Russell S. Ferguson, 12 pages, 10 cents

Encouraging Aspects of Cancer Control, Frank E. Adair, 8 pages, 10 cents

Cancer of the Larynx, Louis H. Clerf, 8 pages, 15 cents

23. *Hay Fever.*—An attractive exhibit combining animation, three dimensional specimens and tinted and illuminated transparencies of the spring and summer offenders and also the frequent autumn hay fever offenders. Some of the spring and summer offenders shown are the box elder, cottonwood, June grass and timothy, while in the autumn section the giant ragweed, the cocklebur, the Russian thistle and the pigweed are shown.

This exhibit is presented with the cooperation of the University of Illinois College of Medicine. Minimum space required, an area 10 feet long by 7 feet deep. More advantageous showing can be made in a space 15 to 20 feet long and 6 feet deep. Electrical connections, three outlets using 800 watts. Shipping weight, 576 pounds.

Literature available from the American Medical Association Order Department:

Asthma, Alene S. and Robert P. Little, 11 pages, 15 cents

What We Know About Allergy, Louis Tuft, 12 pages, 10 cents

Idiosyncrasy, Elliott R. Weyer, 4 pages, 5 cents

Ragweed and Hay Fever, Pollen Map, 4 pages, 5 cents

House Dust Allergy, Karl D. Figley, 8 pages, 15 cents

Protecting Your Child from Allergy, William Gayle Roberts, 8 pages, 10 cents

26. *How Disease Bacteria Are Spread.*—A transparency case shows the size and appearance of bacteria, including the ball-shaped "cocccus," the rod-shaped "bacillus" and the spiral-shaped "spirochete." Also presented in the same transparency case are "bacteria" and "virus." The side panels set forth the ways in which man, animals, insects and foods spread bacteria. Prominently shown is the spread of disease through coughing and sneezing, the spread by rats and other animals, by insects such as flies, mosquitoes, fleas and lice, ticks and mites. One panel shows how disease bacteria are spread through water, milk and other foods, such as improperly home-canned foods and the use of uninspected beef and other meat products.

In the two information files communicable diseases, such as mumps, pneumonia, rabies, smallpox and syphilis, and over 60 other diseases are discussed. Space required, an area 10 feet long by 7 feet deep. No booth background necessary. Electrical connections, one outlet for 240 watts. Shipping weight, 422 pounds.

Literature available from the American Medical Association Order Department:

The House Fly, Claude Lillingston, 4 pages, 10 cents

The Menace of the Rat, Thomas G. Hull, 8 pages, 15 cents

What Everyone Should Know About Milk, Saretta G. Hicks, 8 pages, 15 cents

Shall We Pasteurize? W. W. Bauer, 16 pages, 10 cents

The Raw Milk Menace, Harold J. Harris, 6 pages, 10 cents

Pure Water, the Best of All Drinks, Prof. George C. Whipple, revised by Stanley Osborn, 6 pages, 10 cents

What to Do About Colds, Audrey McKeever, 12 pages, 15 cents

27. *Food Poisoning and Food Borne Infections.*—The four principal avenues of food poisoning and infection are graphically portrayed, namely, chemical food poisoning, bacterial food poisoning, food borne infections and poisonous plants and animals. The central attraction is a transparency case showing the time elapsing between the time of eating poisoned food and the first onset of symptoms. A question box and an information file are shipped with the exhibit. Written questions deposited by visitors in the question box will be answered by the Bureau of Health Education of the American Medical Association. Over 30 of the most frequently asked questions on food poisoning are answered in the information file.

Space required, an area 10 feet long by 6 feet deep. No background necessary. Electrical connections, one outlet using 240 watts. Shipping weight, 410 pounds.

Literature available from the American Medical Association Order Department:

Botulism, Thomas G. Hull, 4 pages, 10 cents

Are Pesticides Making Your Food Unsafe, James R. Wilson, 4 pages, 15 cents

This Little Pig—Trichinosis, David O. Woodbury, 2 pages, 5 cents

Food Poisoning and Food-Borne Infections, Thomas G. Hull, 3 pages, one copy free

28. *Disease Transmitted from Animals to Man.*—The visitor's attention is immediately attracted to the center transparency panel showing insects that carry disease from the animal host to man. The symptoms of some of the diseases transmitted by several animals to man are shown. The role of common domesticated birds and animals, as well as the wild animals, in the transmission of disease to man is shown.

Two information files containing the answers to over 60 common questions on the subject are included with the exhibit. Space required, an area 10 feet long by 7 feet deep. No booth background necessary. Electrical connections, one outlet for 160 watts. Shipping weight, 407 pounds.

Literature available from the American Medical Association Order Department:

The House Fly, Claude Lillingston, 4 pages, 10 cents

The Menace of the Rat, Thomas G. Hull, 8 pages, 15 cents

Diseases Transmitted from Animals to Man, Thomas G. Hull, 6 pages, one copy free

36. *Trichinosis.*—The cause, prevention and signs of trichinosis are set forth in this exhibit. Emphasis is placed on the role of the hog as the principal animal host of the disease. The center illuminated panel is devoted to showing the life cycle of the organism causing trichinosis. Space required, an area 10 feet long by 4 feet deep. Electrical connections, none. Shipping weight, 236 pounds.

Literature available from the American Medical Association Order Department:

This Little Pig—Trichinosis, David O. Woodbury, 2 pages, 5 cents

40. *The Menace of Rats.*—The diseases carried by rats, as well as the geographic distribution and control of these rodents, is presented by means of charts and photographs. An illuminated center case shows dog fleas, cat fleas, Indian rat fleas, mice fleas and other types found on rats. Fifteen diseases carried by rats are shown by means of photographs and drawings. Both the cause and the transmission of each disease is portrayed. On the subject of the control of rats, the following phases are presented: rat proofing, rat destruction and the prevention of breeding.

Two information files give facts and figures on over sixty questions relating to the problem of rats and disease. Space required, an area 10 feet long by 7 feet deep. No booth background necessary. Electrical connections, one outlet using 240 watts. Shipping weight, about 413 pounds.

Literature available from the American Medical Association Order Department:

The Menace of the Rat, Thomas G. Hull, 8 pages, 15 cents

Diseases Transmitted from Rats to Man, Thomas G. Hull, 2 pages, one copy free

46. *Food Fads and Fallacies.*—The center of interest in this exhibit is found in the illuminated transparencies emphasizing "Deficiencies in Food Requirements Result in Malnutrition." Shown in the transparencies are children with rickets, patients with pellagra and certain cases of vitamin deficiency. Side panels emphasize "food foolishness," including such fads as food powders, fruit juice diets as obesity cures and one of the old ideas that milk cannot be taken with many other foods. In the section entitled, "It Is Not So," the fallacy that hard

water hardens the arteries is deprecated. Another fallacy put under the spotlight is an old one that the intake of large quantities of water would "flush" the kidneys. Other food fads that are put in their proper perspective are the raw nut fad and the fallacy that proteins and carbohydrates cannot be taken at the same meal. Interested visitors can obtain detailed information from the information file on such subjects as aluminum poisoning, grape diet, nutmeg as a brain stimulant and similar subjects.

Space required, an area 10 feet long by 6 feet deep. No booth background necessary. Electrical connections, one outlet using 300 watts. Shipping weight, 421 pounds.

Literature available from the American Medical Association Order Department:

Watch Your Diet, E. M. Geraghty, 8 pages, 10 cents

Get the Vitamins You Pay For, Amelia Lautz, 2 pages, 10 cents

The Compatible Eating Fad, Clarence Wm. Lieb, 4 pages, 10 cents

Food Chart, a booklet containing eight charts showing the contribution of typical portions of individual foods in terms of the minimum dietary requirements developed by the Food and Drug Administration, 20 pages, 10 cents

When You're Canning at Home, Doris McCray, 4 pages, 5 cents

100 Calorie Portions of Common Foodstuffs, a pocket-size guide prepared by the American Medical Association's Council on Foods and Nutrition, 8 pages, 5 cents

Safe and Sane Reducing, Maurice Hardgrove, Amalia Lautz and Phoebe M. Walters, 20 pages, 15 cents

How to Gain Weight, Laura A. Miller, 16 pages, 15 cents

Botulism, Thomas G. Hull, 4 pages, 10 cents

47. *Mechanical Quackery.*—This is an exposé of mechanical quackery from the Bureau of Investigation of the American Medical Association. Everything from a "magic horse collar," claimed to magnetize the iron in the blood, to a radioactive "rejuvenator" is presented by display of the actual quack device. Many other wierd and humorous fake gadgets are shown.

An extensive information file is incorporated as a part of the exhibit and contains descriptions and information concerning many more mechanical gadgets. Space required, an area 18 feet wide for a table, with a wall space above for 12 panels, each 22 x 28 inches. Electrical connections, two. Shipping weight, approximately 600 pounds.

58. *Nutritional Deficiencies.*—This exhibit is presented by the Council on Foods and Nutrition of the American Medical Association in conjunction with the Food and Nutrition Board of the National Research Council. Three cases of kodachrome transparencies show "Signs Frequently Associated with Deficiencies of the Dietary Essentials." Typical of the editorial content is the following phrase, which appears in one of the transparency cases: "The pictures above and to the left show various stages in the development of eye lesions in subjects who have long been on deficient diets. Deficiencies of single food essentials are seldom found. A full diet of carefully selected and prepared foods is the best preventive of deficiency state now known." Some of the diseases are pellagra, pernicious anemia complicated with nicotinic acid deficiency. Block charts show the sources of vitamin $B_1$, vitamin G, nicotinic acid, protein, vitamin A, calcium, vitamin C and iron.

Contained in the information file is material dealing with such subjects as daily meals, coffee and tea, meat roughage, sugar and vegetables, a total of over 30 informative statements. Space required, an area 20 feet wide by 6 feet deep; no background necessary. Electrical connections, three outlets using 1,200 watts. Shipping weight, 653 pounds.

Literature available from the American Medical Association Order Department:

Watch Your Diet, E. M. Geraghty, 8 pages, 10 cents

Get the Vitamins You Pay For, Amalia Lautz, 2 pages, 10 cents

The Compatible Eating Fad, Clarence Wm. Lieb, 4 pages, 10 cents

Food Charts, a booklet containing eight charts showing the contribution of typical portions of individual foods in terms of the minimum dietary requirements developed by the Food and Drug Administration, 20 pages, 10 cents

When You're Canning at Home, Doris McCray, 4 pages, 5 cents

100 Calorie Portions of Common Foodstuffs, a pocket-size guide prepared by the American Medical Association's Council on Foods and Nutrition, 8 pages, 5 cents

Safe and Sane Reducing, Maurice Hardgrove, Amalia Lautz and Phoebe M. Walters, 20 pages, 15 cents

How to Gain Weight, Laura A. Miller, 16 pages, 15 cents

Botulism, Thomas G. Hull, 4 pages, 10 cents

60. *Physicians and Schools—School Health Service.*—This exhibit from the Bureau of Health Education of the American Medical Association portrays some of the contributions made by the physician as he works with other personnel in the school health program. It lists a number of the factors to be considered in health guidance of pupils, points out pertinent aspects of emergency care, stresses the need for adjustments in the school program to meet the individual needs of pupils and outlines some of the important phases of communicable disease control in schools. The structure of the advisory school health council is pictured and the importance of medical society participation in the council's activities is emphasized.

Space required, an area 10 feet wide by 6 feet deep, no background necessary. Electrical requirements, none. Shipping weight, 203 pounds.

Literature available from the American Medical Association Order Department:

Suggested School Health Policies, 46 pages, 25 cents, free to persons engaged in health education

Physicians and Schools, 22 pages, 15 cents

Health Inspection of School Children, manual of instructions, 22 pages, 10 cents

Individual Record Blanks for Recording Inspection, each, 5 cents

Individual Height-Weight Record Card, 10 cents

Suggestions for the Teacher's Use of the Individual Height-Weight Record Card, 5 cents

Physical Growth Record Form for Boys (Girls), 5 cents each (specify boy's or girl's form)

Mental Hygiene in the Classroom—How Would You Help a Child Like This? 70 pages, 15 cents

Sanitary Requirements for School Lunches, statement by Joint Committee, 4 pages, 10 cents

Schedule Fatigue in School Children, Joint Committee, 4 pages, 10 cents

The Teacher's Role in Mental Hygiene, Herman M. Jahr and Fred V. Hein, 12 pages, 15 cents

Health Appraisal of School Children, Joint Committee, 29 pages, 15 cents

61. *Examining the School Child.*—This is an exhibit from the Bureau of Health Education of the American Medical Association. Charts, pictures and transparencies show the part of parents and teacher in preparing for the examination, the part of physician and nurse in following up the examination and the advantages of the 15 minute examination together with some of the disadvantages. Space required, an area 10 feet long by 6 feet deep. No booth background is necessary. Electrical requirements, one outlet using 300 watts. Shipping weight, 290 pounds.

Literature available from the American Medical Association Order Department:

Suggested School Health Policies, 46 pages, 25 cents, free to persons engaged in health education

Physicians and Schools, 22 pages, 15 cents

Health Inspection of School Children, manual of instructions, 22 pages, 10 cents

Individual Record Blanks for Recording Inspection, each, 5 cents

Individual Height-Weight Record Card, 10 cents

Suggestions for the Teacher's Use of the Individual Height-Weight Record Card, 5 cents

Physical Growth Record Form for Boys (Girls), 5 cents each (specify boy's or girl's form)

Mental Hygiene in the Classroom—How Would You Help a Child Like This? 70 pages, 15 cents

Sanitary Requirements for School Lunches, 4 pages, 10 cents

Schedule Fatigue in School Children, Joint Committee, 4 pages, 10 cents

The Teacher's Role in Mental Hygiene, Herman M. Jahr and Fred V. Hein, 12 pages, 15 cents

Health Appraisal of School Children, Joint Committee, 29 pages, 15 cents

# MEDICAL LEGISLATION

## FEDERAL

### Universal Military Training

Senator Russell of Georgia introduced for himself and 11 other senators S. 1, which would establish a universal military training program. An amendment in the nature of a substitute was introduced during Senate hearings on this bill. The primary medical importance of this substitute bill is that it would provide a program of physical and mental rehabilitation for those persons who fail to meet military standards and who will voluntarily accept such rehabilitation; the doctor draft would be modified and extended until June 30, 1953, and the length of service would be increased from 21 to 27 months; a minimum of 75,000 students each year, some of whom would be medical students, would be deferred from induction for the purpose of attending schools.

### Federal Aid to Medical Education

A federal aid to medical education bill, S. 337, providing an emergency five year program of grants and scholarships for education in the fields of medical, osteopathy, dentistry, dental hygiene, public health and nursing professions, was introduced by Senator Murray (Montana) for himself and six other senators, all members of the Senate Labor and Public Welfare Committee. It attempts to meet immediately the prospective requirements of the armed forces. Federal assistance could reach 50 per cent of the total cost of instruction. There is a provision to allow medical schools $500 for each medical student up to average enrolment and an additional $500 for such students over average enrolment. This bill is somewhat similar to a federal aid to medical education bill (S. 1453) passed by the Senate during the Eighty-First Congress.

### Local Public Health Units

Fifteen Senators of both parties introduced S. 445, which would authorize assistance to states and their subdivisions in the development and maintenance of local public health units. This bill is identical with S. 522, introduced by Senator Hill (Alabama), which passed the Senate during the last Congress. H. R. 274 provides federal assistance to local health units in defense areas and restricts the types of services to be rendered. It is a revised version of H. R. 5865, which failed to pass the House in 1950.

### Reorganization of Executive Departments

Senator McClellan of Arkansas introduced for himself and six other senators S. 101, which would amend the Reorganization Act of 1949 in regard to any reorganization related to the national security or defense effort by requiring that each such reorganization plan submitted shall (*a*) be certified by the President in his message of transmittal to the Congress as in behalf of the military or war effort; (*b*) be temporary; (*c*) become effective if not vetoed by a vote of House or Senate within a period of 15 days (in place of the present 60 days), and (*d*) remain in force until June 30, 1952, or until termination of the national emergency proclaimed by either the President or Congress, whichever date is the earlier. This bill forbids the President to (1) abolish or transfer an executive department, (2) establish any new executive department, (3) change the name of any executive department or the title of its head and (4) designate any agency as a department or its head as a secretary, even though such a change was declared by the President to be in behalf of the war effort. Representative Holifield of California introduced H. R. 1545, which is a similar bill.

### Medical and Hospital Service for Government Employees

A bill, S. 401, to make available medical and hospital treatment to civilian federal employees who have had a minimum of 10 years' service was introduced by Senator Langer (North Dakota). This bill would allow the Federal Security Administrator to furnish, within the limits of Public Health Service facilities, free medical and hospital treatment for disability, disease and injury, regardless of how sustained or contracted, for all civilian federal employees who have a minimum of 10 years' service and who cannot afford to defray such necessary expenses. The same author introduced S. Res. 25, which is a resolution calling for a study into the desirability and feasibility of instituting a hospitalization program for the benefit of civilian government employees by a health prepayment plan which would also provide surgical costs in hospitals by physicians of the employees' choice. The Senate Committee on Post Office and Civil Service is directed to complete its study and submit a report and recommendations by May 1, 1951.

### Reserve Officers' Training Corps

Senator Russell of Georgia introduced S. 325, and Representative Brooks of Louisiana introduced H. R. 1168, which are identical. These bills rewrite the law respecting Reserve Officers' Training Corps and were introduced at the request of the Secretary of Defense. Among other things, the bills provide medical care for ROTC members in all types of training, whether under the "Career Officer Procurement Program" or the "Non-Career Programs." The medical service amounts to hospitalization, medical and surgical care in hospitals and at the homes of trainees, providing injury or illness is received in connection with such training.

### Miscellaneous

An act to amend the Public Health Service Act to provide for research and investigation as to the cause, prevention, treatment and possible cure of epilepsy was introduced by Senator Langer as S. 188. This bill would establish a National Epilepsy Institute in the Public Health Service.

Representative Rankin of Mississippi introduced H. R. 1081, which would make studies and analyze hospital activities and programs in order to prevent overlapping, duplicating and overbuilding of services and would otherwise look into new hospital construction and wide utilization of existing facilities. The board would make recommendations to the President regarding new hospital construction.

A bill, H. R. 1174, introduced by Representative Davis of Tennessee would authorize the President to appoint as commissioned officers in the Medical Corps of the Army and the Navy, x-ray technicians who are recommended by the Surgeon General of the respective service.

Representative Dingell of Michigan introduced H. J. Res. 68, providing for the establishment and maintenance of a nationwide whole blood and plasma bank as a measure of protection against atomic warfare or other major disaster. This resolution grants authority to the President to establish such a blood bank in the Public Health Service, which would cooperate with the American Red Cross. It also provides for storing and making available whole blood and plasma for public use in the event of atomic warfare or other disaster.

A physical fitness and training program under the auspices of the Civilian Defense Program, or such other agency of government as the President deems advisable, is provided for in H. Con. Res. 19, introduced by Dr. Hedrick, Representative from West Virginia.

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The summary of federal legislation was prepared by the Washington Office of the American Medical Association and the summary of state legislation by the Bureau of Legal Medicine and Legislation.

## STATE

### Arkansas

**Bill Introduced.**—S. 30, to amend **the chiropractic act,** proposes to add the following subjects to the list of those in which chiropractors must be examined: anatomy, chiropractic, diagnosis, hygiene, obstetrics, pathology and roentgenology. The proposal also would omit from the existing law a provision that the chiropractic license shall entitle the holder to adjust by hand the displaced segments of the vertebral column and any displaced tissue in any manner related thereto for the purpose of removing any injury, deformity or abnormality of human beings. This proposal would also omit from the existing law the proviso permitting the board of chiropractic examiners to revoke a license when the licensee prescribes medical treatment.

### Arizona

**Bill Introduced.**—H. 34, proposes to amend the law relating to the **practice of naturopathy** by, among other things, defining naturopathy as a system of the healing arts, embracing prevention, diagnosis, care and treatment of human physical and mental ills, diseases, trichomas, and deformities, by the use and prescription of substances of plant, animal or mineral origin as are naturally found in and required by the human body, herbs, cell salts, plants, roots, barks, mineral and vegetable oils, antiseptic, germicidal and bacteriostatic agents, non-habit forming anodynes, vitamins, and other natural methods, the practice of natural obstetrics, and simple minor surgery, and includes the use of physical, electrical, hygiene and sanitary measures incident thereto, but shall not include major surgery.

### California

**Bill Introduced.**—S. 129, to amend the **health and safety code,** proposes to authorize the state department of public health to prescribe and promulgate minimum standards of safety and sanitation in the physical plant and of diagnostic, therapeutic and laboratory facilities for public medical institutions and to certify to the state department of social welfare the institutions which meet such standards.

### Colorado

**Bills Introduced.**—H. 33, proposes to repeal that portion of **the chiropractic act** which requires chiropractors to take a certain amount of post-graduate education each year in order to obtain annual registration. S. 24, proposes certain amendments to **the basic science act** relating to licenses by reciprocity and other matters. S. 28, proposes to amend **the chiropractic act** by, among other things, permitting the chiropractic board to license chiropractic hospitals and sanatoria and to issue reasonable rules and regulations prescribing minimum standards for the maintenance and operation of such institutions.

### Connecticut

**Bill Introduced.**—S. 10, to amend the temporary disability law, **proposes to define physician** as an individual licensed to practice medicine, chiropody or dentistry under the laws of this or any other state, or a practitioner of healing through prayer or spiritual means, as recognized by a widely established religious denomination.

### Georgia

**Bill Introduced.**—H. 115, proposes to authorize the board of medical examiners to examine and license applicants desiring to **practice physical therapy** and defines physical therapy as the treatment of any bodily or mental condition of any person by the use of the physical, chemical, and other properties of heat, light, water, electricity, massage and active and passive exercise. The use of roentgen rays and radium for diagnostic and therapeutic purposes, including cauterization, are not authorized under the term physical therapy as used in the proposal.

### Illinois

**Bill Introduced.**—S. 11, **to regulate admission of students** to the college of medicine of the University of Illinois, proposes that each class of first-year students shall include at least two residents of each senatorial district in the state providing there are two or more applicants from such district who possess the minimum qualifications.

### Indiana

**Bill Introduced.**—H. 85, proposes the creation of a committee to study, investigate and report on the subject of licensing and regulating **the practice of chiropractic** in Indiana.

### Iowa

**Bills Introduced.**—H. 102 and S. 96, propose to increase the course of **study in chiropractic colleges** from three years to four years and not less than four thousand (4000) sixty- (60) minute hours in actual resident attendance.

### Maine

**Bill Introduced.**—S. 46, proposes an enabling act for the regulation of non-profit **medical service plans.**

### Maryland

**Bill Introduced.**—S. 15, proposes the creation and establishment of a **commission on alcoholism** to make studies and research in the care and treatment of alcoholics.

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The above items were prepared by the Bureau of Legal Medicine and Legislation.

### Massachusetts

**Bill Introduced.**—H. 1202, proposes the establishment of a **blood donation commission** and proposes further that all citizens shall register with the commissioner and their blood shall be catalogued as to type.

### Minnesota

**Bill Introduced.**—S. 63, proposes the creation of a state board of examiners of **psychologists.** The practice of psychology is not defined by the proposal.

### Missouri

**Bill Introduced.**—S. 14, proposes, among other things, the creation of a physician-patient privilege under **a revised evidence act.**

### Montana

**Bill Introduced.**—H. 35, proposes that a physician or surgeon who, whether in the course of the practice of his profession or otherwise, shall, by administration of drugs or by committing an act or series of acts on the person of another, cause the life or health of such other person to be endangered, shall be **guilty of malpractice,** which is declared to be a felony punishable by imprisonment or fine or both. The proposal would further provide that nothing in it should be construed to prohibit any physician or surgeon from administering medicine or otherwise treating his patients in cases where the effect of the medicine or treatment might be dangerous to life or injurious but the administration thereof is in accordance with sound approved medical practice. **(Killed Jan. 22, 1950.)**

### New Mexico

**Bill Introduced.**—H. 11, proposes that every hospital shall post in each room and in the main business office of the hospital a detailed printed list of all **charges for, board and medical supplies** to be charged to each patient or patients who hire a room by the day or month in said hospital.

### New York

**Bills Introduced.**—A. 513, proposes that the state commissioner of health shall supervise and license private, unincorporated **maternity hospitals.** A. 525, proposes that any person licensed to practice a profession who has been **inducted into the military service** any time prior to July, 1952, may have three months after the termination of such service in which to apply for a renewal of his license without examination, fine or penalty. S. 387, proposes that it shall be unlawful for any person to sell at retail or give away any **antihistamine drug or** any other preparation containing antihistamines without obtaining a prescription from a duly licensed practitioner of medicine.

**Bill Enacted.**—A. 19, has become chapter 1 of one of the laws of 1951. It provides regulations for the establishment and operation of **county tuberculosis hospitals.**

### North Carolina

**Bill Introduced.**—H. 43, proposes to amend the law **relating to chiropody** by, among other things, defining chiropody as the diagnosis and medical or surgical or mechanical or manipulative or electrical treatment of all ailments of the human foot and leg. A chiropodist as defined by this proposal is a physician and surgeon of the human foot and leg.

### Ohio

**Bill Introduced.**—H. 68, proposes the establishment within the department of health of a **division of alcoholism** to promote and conduct studies on alcoholism and on the rehabilitation and care of alcoholics.

### Oklahoma

**Bills Introduced.**—H. 30, proposes regulations for the automatic suspension of a license to practice medicine and surgery upon failure **to pay annual registration** for three consecutive years and further proposes the circumstances under which such license may be reinstated. H. 73, proposes that the general sale of patented medicine containing more than 10 per cent **alcohol by volume** shall be prohibited except upon prescription of a duly licensed physician.

### South Dakota

**Bill Introduced.**—H. 66, proposes to authorize **the performance of an autopsy** by a physician or surgeon when authorized (a) by the decedent during his life time or (b) by the decedent's surviving spouse or (c), if the surviving spouse is incompetent or not available or if there be no surviving spouse, by an adult child, parent, brother or sister of the decedent.

### Utah

**Bills Introduced.**—H. 37, proposes the regulation of **non-profit medical service plans** by the insurance department. S. 58, proposes the creation of a **state board of alcoholism** to initiate, develop and administer programs and facilities for the study, treatment and rehabilitation of alcoholics.

### Washington

**Bill Introduced.**—H. 13, proposes certain amendments to **the chiropractic act** among which is an amendment to the definition providing that the practice of chiropractic is the determination of vertebral subluxations by scientific methods and adjusting by hand any articulation of the spine.

### Wyoming

**Bill Introduced.**—H. 39, proposes the creation of a **board of naturopathic examiners** and defines naturopathy as a therapeutic system embracing a complete physianthropy, employing nature's agencies, forces, processes, and products, except major surgery or obstetrics.

# MEDICAL NEWS

## CALIFORNIA

**Annual Medical Evangelists Convention.**—The annual postgraduate convention of the College of Medical Evangelists will be held at the Biltmore Hotel, Los Angeles, March 11-16. Diagnosis, Management, and What's New will be the theme of the lectures and panel discussions. Among the speakers will be:

Robert S. Stone, San Francisco, Individual Protective Measures from an A-Bomb Explosion.
Charles C. Higgins, Cleveland, Present Day Management of Renal Lithiasis.
Chester S. Keefer, Boston, Selection of Anti-Infective Agents in the Prevention and Treatment of Disease.
Maxwell M. Wintrobe, Salt Lake City, Diagnosis and Treatment of Anemias.
Arthur W. Proetz, St. Louis, Clinical Importance of Respiratory Air Currents.
Frederick J. Stare, Boston, Intravenous Fat Feeding.
Alton Ochsner, New Orleans, Diagnosis and Treatment of Carcinoma of Lung.

The last three days of the convention will consist of concentrated courses in the specialties. The registration fee for the convention is $10 and for the special courses $15.

## COLORADO

**Institute on Newborn and Premature Infant Care.**—This institute, to be given February 5-8 at the University of Colorado School of Medicine, Denver, is sponsored by the university and the State Department of Public Health. Guest speakers are Dr. Willard M. Allen, Washington University, St. Louis; Dr. Frederick M. Kriete, San Francisco; Dr. Arthur J. Lesser, U. S. Children's Bureau, Washington D. C., and Dr. Myron E. Wegman, New Orleans. The rest of the faculty will be selected from the University of Colorado School of Medicine, Regional Office of the U. S. Children's Bureau, City and County of Denver Health Department and the State Department of Health. Presentations will be planned so that physicians, hospital administrators, nurses and public health workers may benefit. The registration fee is $10, but there will be no tuition charge. Applications should be sent to the Director of Graduate and Postgraduate Education, University of Colorado School of Medicine, 4200 East Ninth Avenue, Denver 7.

## CONNECTICUT

**Dr. Fulton Becomes Professor of Medical History.**—Dr. John F. Fulton, has been named to fill the newly created position of Sterling Professor of the History of Medicine at Yale University, New Haven. He has relinquished his former duties as Sterling Professor of Physiology and chairman of the department of physiology. He will, however, be at liberty to continue with certain phases of his physiological research.

## ILLINOIS

**Occupational Therapy Scholarships.**—A scholarship fund for the training of students in occupational therapy has been established at the University of Illinois College of Medicine by the Illinois Association for the Crippled. The scholarships are to be given to needy and deserving students who have reached their final year of study in the occupational therapy curriculum.

### Chicago

**Society News.**—The Chicago Urological Society held a symposium on the artificial kidney on January 25. Speakers were Dr. Heinrich Necheles, Dr. S. Howard Armstrong Jr., Dr. Walter M. Kearns, Milwaukee, Dr. Isidore Rochlin and Dr. Virgil A. Place. The society heard also Dr. J. Kenneth Sokol read his candidate's thesis, "Renal Cyst or Tumor?"

**Heart Association Meeting.**—The clinical section of the Chicago Heart Association will hold a meeting at 10: 00 a. m. February 9 at Children's Memorial Hospital. Speakers will be:

Harvey White and Stanley Gibson, Clinical and Angiocardiographic Evaluation in Problem Cases of Congenital Heart Disease.
Frank R. Johnson, Endocardial Fibroelastosis.
William L. Riker, Studies of Growth of Blood Vessel Anastomosis.
Katherine C. Lewis, Incidences of Arrhythmias During Anesthesia.
Jakub G. Schlichter, Electrocardiogram and Congenital Disease.

**Annual Clinical Conference.**—The Chicago Medical Society will hold its annual clinical conference March 6-9 at the Palmer House. Visiting speakers include:

Daniel C. Elkin, Emory University, Ga., Vasodilator Drugs in Peripheral Vascular Disease.
Robert A. Moore, St. Louis, Diseases of the Prostate in Older Persons.
Esmond R. Long, Philadelphia, Immunologic Considerations in Tuberculosis, with Special Reference to Vaccination.
Russell N. DeJong, Ann Arbor, Mich., Headaches, Causes and Treatment.
William W. Scott, Baltimore, Treatment of Cancer of the Urinary Bladder.
H. Dabney Kerr, Iowa City, Diagnosis and Treatment of Carcinoma of the Cervix.
Herbert M. Evans, Berkeley, Calif., Hormones of the Anterior Hypophysis.
William F. Mengert, Dallas, Texas, Simplified Obstetric and Gynecologic Care.
Albert B. Sabin, Cincinnati, Epidemiology of Poliomyelitis.
Orvar Swenson, Boston, Operative Treatment of Hirschsprung's Disease.
Adolph L. Sahs, Iowa City, Diagnosis and Treatment of Meningitis.
Robert D. Dripps Jr., Philadelphia, Postlumbar Puncture Headache, Its Prophylaxis and Treatment.
Robert L. Sanders, Memphis, Tenn., Management of Lesions of Colon.
Francis W. Lynch, St. Paul, Dermatologic Problems in Children.
Conrad G. Collins, New Orleans, Ectopic Pregnancy.
Fred J. Hodges, Ann Arbor, Mich., Roentgen Examination of the Colon—A Badly Neglected Procedure.
L. Emmerson Ward, Rochester, Minn., Use of Cortisone in Rheumatic Diseases.
William T. Green, Boston, Fractures of the Elbow in Children.
Reed M. Nesbit, Ann Arbor, Mich., Common Errors in Diagnosis of Hydronephrosis.
Thomas Hale Ham, Cleveland, Diagnosis and Treatment of Anemia.
Harry L. Parker, Rochester, Minn., Involuntary Movements of the Muscles.
Keith S. Grimson, Durham, N. C., Comparative Values of Vagotomy, Banthine and Gastric Resection in the Treatment of Peptic Ulcer.
Chevalier L. Jackson, Philadelphia, Treatment of Esophageal Disease.
Joseph Stokes Jr., Philadelphia, Virus Diseases in Children.
Paul B. Beeson, Emory University, Ga., Effects of ACTH and Cortisone on Infectious Processes.
Louis A. Brunsting, Rochester, Minn., Disseminated Lupus Erythematosus.
H. Marvin Pollard, Ann Arbor, Mich., Early Diagnosis of Gastric Carcinoma.

Daily round-table luncheon discussions will be held. Panel discussions closing the sessions each afternoon except Tuesday will be on "What's New in Medicine and Surgery," "Cardiology," and "ACTH," respectively. Exhibits will be shown. The registration fee is $5.

## INDIANA

**Heart Symposium.**—The second annual heart symposium for practicing physicians, presented by the Indiana University School of Medicine, Bloomington-Indianapolis, in cooperation with the Indiana Heart Foundation, will be presented on February 14 in the medical school auditorium, Indianapolis, from 10:00 a. m. to 5:00 p. m. This symposium is open to all physicians without advance registration or fees.

**Lectures on Cancer.**—The Indiana University School of Medicine, Indianapolis, is giving a series of lectures and discussions on cancer. The series was initiated in January when Dr. Isadore Lampe, University of Michigan Medical School, Ann Arbor, participated in a two day series of radiology conferences. Dr. Robert E. Stowell, department of oncology, University of Kansas School of Medicine, Lawrence-Kansas City, will deliver two lectures at the Medical Center on February 16, discussing the histochemistry in cancer research and histochemical studies of normal and neoplastic livers. Third in the series of speakers

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.

will be Dr. Howard R. Bierman, University of California Medical School, San Francisco. The program, directed by Dr. Edwin A. Lawrence, has the support of the Indiana Cancer Society.

## KENTUCKY

**Course on Resuscitation.**—A three day course on the resuscitation of patients in the operating room is being conducted by Dr. Charles S. Beck, Louisville, under the sponsorship of the Cleveland Heart Society. The program was presented in December and January and will be given also February 15-17 and March 15-17.

**Poliomyelitis Aid Received.**—During 1950 the National Foundation for Infantile Paralysis advanced three checks totaling $82,600 to the Kentucky Chapter for the treatment of the state's largest number of poliomyelitis patients. At present the chapter is providing funds for the care of 386 patients stricken in 1950 and 473 stricken in past years.

## MASSACHUSETTS

**Rehabilitation Conference.**—The Bay State Society for the Crippled and Handicapped, Inc., will hold a rehabilitation conference at the Copley Plaza Hotel, Boston, February 21. The morning meeting will include a discussion of the Bay State Society Rehabilitation Projects in Springfield, Worcester and Boston. The luncheon speaker will be Mr. Eugene J. Taylor, New York, assistant professor, department of physical medicine and rehabilitation, New York University College of Medicine. In the afternoon there will be a demonstration clinic showing what is being done in rehabilitation, conducted by Dr. George G. Deaver, Lenox Hill Hospital, New York.

## MICHIGAN

**Postgraduate Clinical Institute.**—The fifth annual Michigan Postgraduate Clinical Institute will be held at the Book-Cadillac Hotel, Detroit, on March 14-16, under the sponsorship of the Michigan State Medical Society, University of Michigan Department of Postgraduate Medicine and the Medical School, Wayne County Medical Society, Wayne University College of Medicine, Michigan Department of Health and the Michigan Foundation for Medical and Health Education. Visiting speakers are as follows:

Allan C. Barnes, Columbus, Ohio, Dietary Therapy in Pregnancy and Its Complications.
Russell S. Boles, Philadelphia, Medical and Surgical Approach to Infectious Diseases of the Colon.
David A. Boyd Jr., Rochester, Minn., Psychological Language of the Organs.
Willis E. Brown, Little Rock, Ark., Management of Edema in Obstetrics and Gynecology.
Stanley Gibson, Chicago, Recognition of Heart Disease in Children.
John E. Gordon, Boston, Epidemiology of Accidents.
Evarts A. Graham, St. Louis, Common Errors in Diagnosis of Bronchiogenic Carcinoma with Special Reference to Virus Pneumonia.
W. Paul Holbrook, Tucson, Ariz., ACTH and Cortisone Panel.
Everett D. Kiefer, Boston, Diagnosis and Treatment of Chronic Small Intestinal Disease.
Francis D. Moore, Boston, Metabolic Response to Surgery, and a participant on ACTH and Cortisone Panel.
Charles A. Ragan Jr., New York, participant on ACTH and Cortisone Panel.
Captain George N. Raines, M. C., U. S. N., Washington D. C., Somatic Manifestations of Depression.
Clement A. Smith, Boston, Management of the Premature Infant.
Willard O. Thompson, Chicago, Androgens and Estrogens in General Practice.
Noyes L. Avery Jr., Grand Rapids, Mich., Pancreatitis, Clinical Manifestations and Treatment.

Dr. Lunette I. Powers of Muskegon will be honored in appropriate ceremony Wednesday evening, which also will feature entertainment for all institute registrants and their guests. Dr. Stafford L. Warren of Los Angeles, Calif., will speak at a public meeting Thursday evening on "Atomic Warfare and Atomic Energy." Special societies and alumni groups meeting coincident with the institute include the Woman's Auxiliary to the Michigan State Medical Society, Michigan Pathological Society, Michigan Proctologic Society, Michigan Regional Committee on Fractures and Other Traumas, American College of Surgeons, Michigan Branch of the Academy of Pediatrics and Detroit Pediatric Society, Wayne University College of Medicine Alumni Association, Michigan Academy of General Practice, Michigan Arthritis and Rheumatism Foundation. A registration of over 2,000 is anticipated.

## NEW JERSEY

**Cancer Bulletin.**—A bimonthly bulletin of cancer progress, entitled *CA*, is being distributed to the physicians of the state. The bulletin condenses for physicians information about diagnosis, treatment control and research before the news reaches the public. Each issue is to contain at least one feature about a specific clinical aspect of cancer, a question and answer section, reports from the literature and a calendar of pertinent meetings. The bulletin is published by the American Cancer Society, New Jersey Division, Inc., 9 Clinton Street, Newark 2.

## NEW MEXICO

**Bubonic Plague.**—Dr. James R. Scott, director of the state department of health, has reported a fatal case of bubonic plague in a man living in Hobbs, Lea County. The diagnosis was confirmed by laboratory examination. In 1950 three cases of bubonic plague were reported in New Mexico, one of which occurred in Lea County in January.

## NEW YORK

**Dr. Kochakian Leaves for Oklahoma.**—Charles D. Kochakian, Ph.D., associate professor of physiology, University of Rochester School of Medicine and Dentistry, has become assistant director of the Research Institute and Hospital of the Oklahoma Medical Research Foundation in Oklahoma City. Dr. Kochakian has been associated with the medical school for the past 17 years as an endocrinologist and physiological chemist.

**Civil Service Examination.**—The New York State Department of Civil Service is holding a nationwide examination for senior supervisor of school medical service (general) on April 14. The entrance salary is $5,650 and there are five annual salary increases, up to the maximum of $6,910. Candidates must be graduates of an approved medical school, must have completed an internship of one year in an approved hospital and must have a license to practice medicine in New York State or be eligible to enter the examination for such license. They must have two years' experience in the practice of medicine, including service as a school physician plus one more year of experience or one year of training in medicine or public health beyond the M.D. degree or an equivalent combination. Application blanks can be obtained from the New York State Department of Civil Service, 39 Columbia Street, Albany. The application fee is $5.

### New York City

**Welch Lecture.**—Dr. Alfred Blalock, Baltimore, delivered the William Henry Welch Lecture of Mount Sinai Hospital, on cardiovascular surgery, January 19.

**Course in Occupational Dermatoses.**—New York University Post-Graduate Medical School will give a course in occupational dermatoses at its Institute of Industrial Medicine February 5-9. Information may be obtained from the Dean, New York University Post-Graduate Medical School, 477 First Avenue, New York 16. The maximum registration is 50, and the tuition fee is $50.

**Civilian Defense Appointments.**—Dr. Ralph S. Muckenfuss, assistant commissioner of health, has been appointed blood services officer for the City of New York, and Dr. Theodore Rosenthal, director of the Bureau of Adult Hygiene, has been appointed as first aid control officer in the Medical Emergency Division of the City Office of Civil Defense. Dr. Muckenfuss will integrate the activities of blood procurement by the American Red Cross, the work of the blood banks in hospitals and the private blood banks in the city. Dr. Rosenthal will supervise the development of the civil defense aid stations. There are being organized at least 400 such units in the city to give professional first aid to the injured prior to their removal to hospitals. Progress has already been made in the training of a large instructor group in New York by a coordinated effort of the state and county medical societies, the medical schools,

the state department of health, the city health and hospital departments and the American Red Cross. A large program of basic training for hospital workers is under way in all hospitals of the city.

## OHIO

**Personal.**—Dr. Sidney Lange, a member of the faculty of the University of Cincinnati College of Medicine, was given an honorary title of professor emeritus of radiology on November 7. He retired September 1.

**Speech and Hearing Center.**—The Cincinnati League for Hard of Hearing has been largely responsible for setting up a Speech and Hearing Center at 616 Walnut Street to deal with the rehabilitation of persons referred. As a member of the community chest it will carry on a public education program on the prevention of speech and hearing disorders. Fees will be commensurate with individual ability to pay.

**Radiation Safety Program.**—Ohio State University has established a program aimed at protecting workers in campus laboratories from the hazards of radiation to help solve the problems created by the steadily mounting use of radiation-generating machines and radioactive materials in the university's research projects. Lester R. Rogers, superintendent of the program, will be responsible for establishing safety measures in all areas of research and study in which generating machines and radioisotopes are used. He will keep records of the receipt and distribution of radioisotopes, make systematic surveys of the laboratories in which they are used, maintain records of blood cell counts of exposed persons and check methods of disposal of radioactive waste materials.

## PENNSYLVANIA

**Dr. Teague Appointed Secretary of Health.**—Dr. Russell E. Teague, senior surgeon in the U. S. Public Health Service and assistant professor of preventive medicine at the University of Pennsylvania, Philadelphia, has been appointed secretary of health for the state of Pennsylvania. Dr. Teague was associated with the Kentucky state department of health from 1939 to 1945 and during the last three of those years was deputy state health officer. He went to Philadelphia as an assistant director of the Henry Phipps Institute and on assignment from the public health service has conducted research in tuberculosis control there.

**Health Poster Exhibit.**—Prize-winning posters in the 1950 Health Poster Contest, sponsored by the Medical Society of the State of Pennsylvania, and health posters from 50 foreign countries were exhibited at the Pennsylvania State Museum, Harrisburg, recently and was viewed by more than 20,000 visitors, of whom 15,000 were children of school age. The exhibition will be shown at the Reading Museum also.

### Philadelphia

**Basic Science Lecture Series.**—A weekly series of lectures to the house staff of the Philadelphia General Hospital dealing with the basic sciences as applied to medicine has been arranged. Speakers are Drs. David L. Drabkin, William E. Ehrich, Seymour S. Kety, professors of biochemistry, pathology, and clinical physiology, respectively, at the Graduate School of Medicine, University of Pennsylvania.

**Promotions at Temple University.**—The following promotions are among those recently approved for the faculty of the Temple University School of Medicine, Philadelphia. Promoted from clinical professor to professors were Dr. George P. Rosemond, in surgery; Dr. Michael Scott, in neurosurgery, and Dr. John Lansbury, in medicine. Dr. Louis A. Soloff, assistant professor, was promoted to associate professor of medicine and Dr. I. George Blumstein, associate, to assistant professor of medicine.

**Personals.**—Dr. Kenneth A. Koerber has been appointed chief industrial physician for Sharp & Dohme. Just prior to his association with the company, he held a civilian post with the U. S. Army Hospital at Fort Eustis, Va. Dr. Koerber succeeds Dr. R. Ralph Bresler, who has resigned to enter private practice. ——Dr. Garfield G. Duncan, Philadelphia, was elected president of the Society of the United States Medical Consultants in World War II at a recent meeting in Washington, D. C.

## TEXAS

**Research Society Meeting.**—Dr. Robert P. Glover of Philadelphia will be the guest speaker at the Baylor Research Society meeting in Houston February 7, talking on new advances in surgery of the heart valves. He is clinical professor of surgery of Hahnemann Medical College, Philadelphia. On the day preceding his Houston talk Dr. Glover will address the Tarrant County Medical Society in Fort Worth.

**Child Development Center Institute for Teachers.**—The University of Texas Child Health Program is presenting a two day institute on child behavior for school teachers in Galveston February 15-17. This institute is being offered by the Child Development Center, under the direction of Dr. C. Christopher Morris II and is designed as an educational service to the community rendered by the faculty of the medical school. Teachers' problems with child behavior will be thoroughly considered and illustrated with clinical demonstrations. Dr. Leo Kanner, director of the Children's Psychiatric Clinic at Johns Hopkins Hospital, Baltimore, will be the guest speaker. School physicians and others interested are advised to communicate with Dr. Arild E. Hansen, Director of the Child Health Program, University of Texas Medical Branch, Galveston.

## HAWAII

**Centennial Report of Health Department.**—In December the Department of Health, Territory of Hawaii, issued its hundredth anniversity report. One hundred years ago it began with one full time health worker and has grown to require the full time health services of more than 600 physicians, engineers, nurses, social workers, sanitarians, laboratory workers and other specialists. Its first appropriation was $10,000 for the prevention of cholera epidemic, and its budget today is more than 300 times that amount. The report lists the progress of various health services of the department and outlines future projects.

## GENERAL

**Studies of Problems of Older People.**—The Rockefeller Foundation has made two grants for studies relating to the adjustments of older people to retirement and other problems of aging: $20,500 to the University of Chicago for the Committee on the Study of Later Maturity and $15,000 to Cornell University, New York, for a preliminary study of social adjustment in old age.

**Mental Hygiene in Comic Book.**—A special mental health edition of the Blondie comic book was made available for national distribution on January 20 from the National Association for Mental Health. Chic Young's popular Bumstead family is featured in four humorous everyday adventures into which basic mental health messages have been subtly interwoven. Originally produced by the New York State Department of Mental Hygiene, the new edition may be secured from the National Association for Mental Health, 1790 Broadway, New York 19.

**Science Writing Awards.**—The American Association for the Advancement of Science—George Westinghouse Science Writing Awards for the best science writing in 1950 were made at the annual meeting December 28 in Cleveland. Awards made for medical writing included the one to Mr. Norman M. Howden, Rochester, N. Y., $1,000 for the best newspaper science writing in 1950. Robert Goldman, now of the New York *Post*, was a member of the staff of the Detroit *Free Press*, when he wrote a series of articles on heart disease that received honorable mention.

**Research Council Grants-In-Aid.**—The Committee for Research in Problems of Sex of the National Research Council expects to have funds available for new grants-in-aid during the fiscal period July 1 to June 30, 1952. Applications

will be received until March 15, 1951. Blanks may be obtained from the Division of Medical Sciences, National Research Council, 2101 Constitution Avenue, Washington 25, D. C. Preliminary inquiries should be addressed to Dr. George W. Corner, chairman of the committee, Carnegie Institution of Washington, Baltimore 5.

**Dr. Loeb Honored.**—The *A. M. A. Archives of Pathology* dedicated its December 1950 issue to Dr. Leo Loeb in recognition of his distinguished and prolific contributions to experimental biology and medicine. Dr. Loeb retired in 1937 from the faculty of Washington University School of Medicine, St. Louis, where he had been professor of pathology and head of the department since 1924, and is currently working on a book, "The Nature and Cause of Cancer." Some of Dr. Loeb's most distinguished students contributed articles for the issue, which contains a bibliography of more than 400 of his own writings.

**Postgraduate Courses in Chest Diseases.**—The Subcommittee for Regional Courses of the Medical Education Committee of the American Trudeau Society has arranged three postgraduate courses in chest diseases. The first, to be held at Albany, N. Y., in cooperation with Albany Medical College, will consist of four two-hour sessions on tuberculosis, other chronic pulmonary conditions, industrial pulmonary problems and cancer of the lung. Sessions will be held weekly beginning March 29 and ending April 19. The second course is scheduled for the week of March 26 in Boston under the chairmanship of Dr. Edward J. Welch of Boston University School of Medicine. A definite date for the third course to be held in Milwaukee has not been set but will be held at about the same time as the Boston course.

**Paraplegia Foundation Fellowships.**—The National Paraplegia Foundation announces the continuation of a limited number of fellowships for research in spinal cord disease and trauma and in the complications commonly associated with such disease or injury. These fellowships carry a minimum stipend of $3,000 per year and may be awarded to any candidate who has demonstrated a capacity for medical research and has outlined a program of meritorious study. The fellowships, awarded by the Medical Advisory Committee, are open for the academic year 1951-1952. Application forms may be obtained from the Chairman of the Medical Advisory Committee, Dr. Leslie W. Freeman, director surgical research, Indiana University School of Medicine, Indianapolis, and should be submitted to him not later than June 1, 1951.

**Surgeons Section Meeting in Virginia.**—The second Sectional Meeting of the American College of Surgeons will be held in Hot Springs, Va., February 26-27, with headquarters at the Homestead. Attendance will be largely from Alabama, Florida, Georgia, Kentucky, North Carolina, South Carolina, Tennessee, Virginia, Washington, D. C., and West Virginia. The sectional meeting will open at 8:30 both mornings with the showing of medical motion pictures. "The Effect of Vasodilator Drugs on the Circulation of the Extremities," "Chest Injuries" and "Fractures about the Ankle Joint" will be discussed at the opening scientific session. Panel discussions the first afternoon will be on neck surgery and peptic ulcer. On the second morning there will be a session devoted to discussion of injuries of the biliary ducts. Panel discussions on emergencies arising during operation and surgery of the colon, anus and rectum will feature the afternoon medical program.

**Infantile Paralysis Fellowships.**—The National Foundation for Infantile Paralysis announces a limited number of predoctoral and postdoctoral fellowships available to candidates whose interests are research and teaching in the fields related to the problems of poliomyelitis, such as virology, biochemistry, biophysics, orthopedics, pediatrics, neurology and epidemiology. Predoctoral fellowships cover a period of one year but may be considered for renewal. Postdoctoral fellowships cover a period of one to three years, with the privilege of renewal depending on the candidate's previous training and his program. Stipends to the fellows will range from $1,200 to $1,800 a year plus tuition for the predoctoral level, to $3,600 to $7,000 a year for the postdoctoral candidates. Marital and dependency status is considered in the determination of the individual stipend. Institutions that accept fellows will receive additional compensation. Eligibility requirements include United States citizenship and sound health. Predoctoral applicants must be candidates for an M.D., Ph.D. or its equivalent. Postdoctoral applicants must have an M.D., Ph.D. or its equivalent. Successful candidates will be designated a "Fellow of the National Foundation for Infantile Paralysis." Complete information concerning qualifications and applications may be obtained from the Division of Professional Education, National Foundation for Infantile Paralysis, 120 Broadway, New York 5.

**Streptomycin Suit Settled.**—Settlement of the suit brought by Albert Schatz, Ph.D., Brooklyn College professor, against Dr. Selman A. Waksman, Rutgers University microbiologist, and the Rutgers Research and Endowment Foundation was announced December 29. Under the terms of the settlement Dr. Schatz retracted his charge that Dr. Waksman had used "fraud and duress" to induce him to assign to the foundation his right in the patent on the drug streptomycin. This was the main point at issue in the litigation. For his part in the discovery of streptomycin Dr. Schatz will receive 3 per cent of the net royalties from the drug beginning Oct. 1, 1950. He will also receive $125,000 for assignment by him of his rights in Canadian, New Zealand, Japanese and all other foreign patent rights to the foundation. Eighty per cent of the royalties will remain in the foundation for further scientific research, including the work of the Institute of Microbiology. Dr. Schatz is one of 26 persons who worked with Dr. Waksman on the discovery and development of streptomycin, all of whom will receive financial recognition for their work. Originally Dr. Waksman had been granted 20 per cent of the net royalties, but when they began to accumulate he voluntarily requested the foundation to cut his share in half. Conclusion of the litigation between Drs. Schatz and Waksman will make it possible for Dr. Waksman to proceed with his plans for a foundation financed from his part of the royalties to support the advancement of microbiologic science throughout the world and for the university to reactivate its plans for a building to house the Institute of Microbiology.

**American Board of Clinical Chemistry.**—A certifying board, the American Board of Clinical Chemistry, Inc., has been established by representatives from the American Chemical Society, Inc., American Institute of Chemists, Inc., and the American Society of Biological Chemists, Inc. Its purpose is to encourage the study, improve the practice, elevate and establish standards and advance the science of that specialized branch of chemistry entitled "clinical chemistry"; to grant and issue certificates or other recognition of special knowledge in clinical chemistry to voluntary applicants who have established their fitness, and to furnish in the public interest a registry of individuals with specialized knowledge in clinical chemistry who have from time to time been granted certificates by the board. The board is analogous in purpose to the medical specialty boards. Requirements for admission to examination and certification are briefly as follows: 1. Presentation of evidence of satisfactory moral and ethical standing. 2. Educational background equivalent to that of a Doctor of Science. 3. Accredited courses in analytical organic, physical and biological chemistry. 4. Either three years' full time experience in an acceptable clinical laboratory or five years in a position of assistant professor or above in biological chemistry, clinical chemistry or related fields. 5. Pass a written and/or oral examination on broad principles of clinical chemistry. 6. Candidates without the full formal educational requirements set forth above but who have practiced clinical chemistry for 10 years in a responsible position in an acceptable clinical laboratory may be certified without examination at the discretion of the board. 7. Candidates who file applications prior to July 1, 1952, whose qualifications based on training and experience satisfy the board, may be certified without examination. Information may be obtained from the secretary-treasurer, Dr. Joseph W. E. Harrisson, 1921 Walnut Street, Philadelphia 3. A fee of $1 must accompany the application request to cover clerical and mailing costs.

## DEATHS IN OTHER COUNTRIES

**Sir Leonard Parsons,** authority on diseases of children, died in Birmingham, England, December 17, aged 71. He began his long career as a lecturer in the Royal College of Surgeons in 1912 and recently gave the Harveian Oration at the Royal College of Physicians and the Harben Lectures at the Royal Institute of Public Health and Hygiene. In 1930 he was vice president of the International Congress of Paediatrics in Stockholm, was president from 1942 to 1945 of the British Paediatric Association and in 1942 was awarded the Moxon Medal by the Royal College of Physicians. He was awarded a knighthood in 1946 in recognition of his fine work for children during the war years.——**Sir William Thomson,** professor of medicine for the last 27 years at Queens University, Belfast, died November 26, aged 65. He was president of the Association of Physicians of Great Britain and Ireland in 1949 and was elevated to a knighthood in the last New Year Honours List.

## CORRECTION

**Propylthiouracil in Thyrotoxicosis.**—In the abstract on this subject in THE JOURNAL of Jan. 13, 1951, page 113, the sentence "Many of the medically treated patients died" should have read "Many of the medically treated patients were lost from observation."

# EXAMINATIONS AND LICENSURE

### BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 26-28. Sec., Dr. D. G. Gill, 519 Dexter Ave., Montgomery.

ALASKA:* Juneau, March 13. Qualified applicants may request a special examination in other towns where board members are located. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARKANSAS: * *Regular.* Little Rock, June 7-8. Sec., Dr. Joe Verser, Harrisburg. *Homeopathic.* Fort Smith, June 7-8. Sec., Dr. Carl S. Bungart, 105 N. 14th St., Fort Smith. *Eclectic.* Little Rock, June 7-8. Sec., Dr. C. H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Written.* Los Angeles, Feb. 26-March 1. *Oral.* Los Angeles, Feb. 24. *Oral and Clinical for Foreign Medical School Graduates.* Los Angeles, Feb. 25. Sec., Dr. Frederick N. Scatena, 1020 N St., Sacramento 14.

CONNECTICUT: * *Examination.* Hartford, March 13-14. Sec. to the Board, Dr. Creighton Barker, 160 St. Ronan St., New Haven. *Homeopathic.* Derby, March 13-14. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

GEORGIA: Atlanta, June. Augusta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. John Y. Battenfield, Agana.

INDIANA: Indianapolis, June 20-22. Exec. Sec., Miss Ruth V. Kirk, 1138 K. of P. Bldg., Indianapolis 4.

IOWA: * *Written.* Iowa City, June 11-13. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Kansas City, June 6-7. Sec., Dr. O. W. Davidson, 864 New Brotherhood Building, Kansas City.

KENTUCKY: Louisville, June 6-8. Sec., Dr. Bruce Underwood, 620 S. 3rd St., Louisville.

MAINE: Portland, March 12-13. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: Baltimore, June 19-22. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 1. *Homeopathic.* Baltimore, June 19-20. *Examination.* Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MISSISSIPPI: Jackson, June. Asst. Sec., Dr. R. N. Whitfield, Jackson 113.

MISSOURI: *Examination.* Jefferson City, Feb. 19-21. *Reciprocity.* Jefferson City, Feb. 12. Ex. Sec., Mr. John A. Hailey, Box 4, Jefferson City.

MONTANA: Helena, April 2-4. Sec., Dr. S. A. Cooney, 214 Power Block, Helena.

NEBRASKA: * June 1951. Director, Mr. Oscar F. Humble, Room 1009, State Capitol Bldg., Lincoln.

NEVADA: Carson City, Feb. 5. Sec., Dr. George H. Ross, 112 Curry St., Carson City.

NEW HAMPSHIRE: *Examination.* Concord, March 14-15. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 19-22. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, April 10-11. Sec., Dr. Charles J. McGoey, Coronado Bldg., Santa Fe.

OHIO: *Endorsement.* Columbus, April 3. Sec., Dr. H. M. Platter, 21 W. Broad Street, Columbus.

OKLAHOMA: * *Examination.* Oklahoma City, June 6-7. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

PUERTO RICO: *Examination.* Santurce, March 6. Sec., Mr. Luis Cueto Coll, Box 3717, Santurce.

SOUTH CAROLINA: *Reciprocity.* Columbia, Feb. 5, March 5, April 2. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

UTAH: Salt Lake City, July 1951. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

VERMONT: Burlington, February 1951. Sec., Dr. F. J. Lawliss, Richford.

VIRGIN ISLANDS: St. Thomas, June 12. Sec., Dr. Earle M. Rice, St. Thomas.

WYOMING: *Examination.* Cheyenne, Feb. 5. Sec., Dr. Franklin D. Yoder, Capitol Bldg., Cheyenne.

### BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* Juneau, February, or when qualified candidates make application. Sec., Dr. C. Earl Albrecht, Box 140, Juneau.

ARIZONA: *Examination.* Tucson, March 20. Sec., Mr. Francis A. Roy, Room 427, Liberal Arts Bldg., University of Arizona, Tucson.

ARKANSAS: *Examination.* Little Rock, May 8-9. Sec., Mr. L. E. Gebauer, 1002 Donaghey Bldg., Little Rock.

COLORADO: *Examination.* Denver, March 7-8. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 3.

CONNECTICUT: *Examination.* Feb. 10. Executive Asst., State Board of Healing Arts, Mr. M. G. Reynolds, 110 Whitney Ave., New Haven 10.

DISTRICT OF COLUMBIA: *Examination.* April 23-24. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.

FLORIDA: *Examination.* Gainesville, June 2. Sec., Mr. M. W. Emmel, University of Florida, Gainesville.

OKLAHOMA: *Examination.* Oklahoma City, March 27. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, March 3. Sec., Mr. Charles D. Byrne, University of Oregon, Eugene.

RHODE ISLAND: *Examination.* Providence, Feb. 14. Chief, Division of Professional Regulation, 366 State Office Bldg., Providence.

TEXAS: *Examination.* Latter Part of April. Sec., Bro. Raphael Wilson, 306 Nalle Bldg., Austin.

WISCONSIN: *Examination.* Madison, April 7. Sec., Mr. W. H. Barber, Scott and Watson Sts., Ripon.

* Basic Science Certificate required.

# MEETINGS

ANNUAL CONGRESS ON INDUSTRIAL HEALTH, Atlanta Biltmore Hotel, Atlanta, Ga., Feb. 26-28. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago 10, Secretary.

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE, Palmer House, Chicago, Feb. 12-13. Dr. Donald G. Anderson, 535 N. Dearborn St., Chicago 10, Secretary.

NATIONAL CONFERENCE ON RURAL HEALTH, Peabody Hotel, Memphis, Tenn., Feb. 23-24. Dr. F. S. Crockett, 535 N. Dearborn St., Chicago 10, Chairman.

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AMERICAN ACADEMY OF ALLERGY, Hotel Statler, New York, Feb. 5-7. Dr. Walter S. Burrage, 208 E. Wisconsin Ave., Milwaukee 2, Secretary.

AMERICAN ACADEMY OF FORENSIC SCIENCES, Drake Hotel, Chicago, March 1-3. Prof. Ralph F. Turner, Michigan State College Dept. of Police Administration, East Lansing, Mich., Secretary.

AMERICAN ACADEMY OF GENERAL PRACTICE, San Francisco, March 19-22. Mr. Mac F. Cahal, 406 W. 34th St., Kansas City 2, Mo., Executive Secretary.

AMERICAN ASSOCIATION OF ANATOMISTS, Detroit, March 21-23. Dr. Normand L. Hoerr, 2109 Adelbert Road, Cleveland 6, Secretary.

AMERICAN COLLEGE OF ALLERGISTS, Edgewater Beach Hotel, Chicago, Feb. 11-14. Dr. Fred W. Wittich, 423 LaSalle Medical Bldg., Minneapolis 2, Secretary.

ASSOCIATED STATE POSTGRADUATE COMMITTEES OF STATE MEDICAL SOCIETIES, Palmer House, Chicago, Feb. 10-11. Dr. Charles W. Smith, 230 State St., Harrisburg, Pa., Secretary.

ATLANTA GRADUATE MEDICAL ASSEMBLY, Municipal Auditorium, Atlanta, Ga., Feb. 5-7. Mrs. Stewart R. Roberts, 768 Juniper St. N.E., Atlanta, Executive Secretary.

CENTRAL SURGICAL ASSOCIATION, Chicago, Feb. 22-24. Dr. James T. Priestley, Mayo Clinic, Rochester, Minn., Secretary.

CHICAGO MEDICAL SOCIETY ANNUAL CLINICAL CONFERENCE, Palmer House, Chicago, March 6-9. Dr. Walter C. Bornemeier, 30 N. Michigan Blvd., Chicago 2, Secretary.

CONFERENCE ON CHRONIC DISEASE—PREVENTIVE ASPECTS, Edgewater Beach Hotel, Chicago, March 12-14. Dr. Morton L. Levin, 535 N. Dearborn St., Chicago, Director.

MICHIGAN POSTGRADUATE CLINICAL INSTITUTE, Book-Cadillac Hotel, Detroit, March 14-16. Dr. L. Fernald Foster, 2020 Olds Tower, Lansing 8, Secretary.

MID-SOUTH POSTGRADUATE MEDICAL ASSEMBLY, Peabody Hotel, Memphis, Tenn., Feb. 13-16. Dr. Thurman Crawford, 899 Madison Ave., Memphis, Secretary.

NATIONAL CONFERENCE ON MEDICAL SERVICE, Palmer House, Chicago, Feb. 11. Dr. R. E. Fitzgerald, 2218 N. Third St., Milwaukee 12, Secretary.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS, Hotel New Yorker, New York, March 28-30. Dr. Franklin M. Foote, 1790 Broadway, New York 19, Executive Director.

NEW ORLEANS GRADUATE MEDICAL ASSEMBLY, Municipal Auditorium, New Orleans, March 5-8. Dr. W. D. Beacham, 1430 Tulane Ave., New Orleans 12, Secretary.

SOUTHEASTERN SECTION, AMERICAN UROLOGICAL ASSOCIATION, Peabody Hotel, Memphis, Tenn., March 7-10. Dr. Russell B. Carson, Sweet Bldg., Fort Lauderdale, Fla., Secretary.

# DEATHS

**Cannon, A. Benson** ⊕ New York; born in Wilcox County, Ala., Nov. 10, 1888; Tulane University School of Medicine, New Orleans, 1913; professor of dermatology at Columbia University College of Physicians and Surgeons; specialist certified by the American Board of Dermatology and Syphilology; member of the American Dermatological Association, American Academy of Dermatology and Syphilology, New York Dermatological Society, New York Academy of Medicine, Sigma Alpha Epsilon, Alpha Kappa Kappa and the Clinical Research Society; affiliated with City Hospital, Neurological Institute and Woman's Hospital in New York, Nassau Hospital, Mineola, Sharon (Conn.) Hospital and Vassar Brothers Hospital in Poughkeepsie, N. Y.; trustee of the Erskine College in Due West, S. C.; died while riding horseback near Millbrook, N. Y., November 27, aged 62, of myocarditis.

**Barnes, Lawson Paul** ⊕ Bennettsville, S. C.; born in Florence, S. C., April 24, 1902; University of Pennsylvania School of Medicine, Philadelphia, 1927; specialist certified by the American Board of Ophthalmology; served during World War II; vice president of Marlboro County Medical Society and the North Carolina and South Carolina Eye, Ear, Nose and Throat Society; surgeon, Marlboro County General Hospital and consulting ophthalmologist at Scotland County Memorial Hospital, Laurinburg, N. C.; surgical oculist with the Seaboard Air Line Railway; president of the local Rotary Club; died in Columbia while watching a football game November 18, aged 48, of coronary thrombosis.

**Elam, William Tecumseh,** St. Joseph, Mo.; born in 1866; Northwestern Medical College, St. Joseph, 1890; fellow of the American College of Surgeons; member of the American Urological Association; formerly vice president of the state board of health; member of the American Medical Association and in 1927 a member of its House of Delegates; past president of the Buchanan County Medical Society; served during World War I; affiliated with Missouri Methodist Hospital and St. Joseph's Hospital; died November 20, aged 84, of gastrointestinal hemorrhage.

**Amiss, Emil Parke,** Martinsville, Va.; University College of Medicine, Richmond, Va., 1898; died November 3, aged 78, of chronic glomerular nephritis.

**Anderson, Clyde Maxwell** ⊕ Hermosa Beach, Calif.; Medico-Chirurgical College of Philadelphia, 1915; served as vice president and for many years as member of the council of the Los Angeles County Medical Society; at one time surgeon in charge at Natchez (Miss.) Charity Hospital; founder and organizer of the Hermosa-Redondo Hospital, later known as the South Bay Community Hospital; died November 21, aged 64, of coronary occlusion.

**Anderson, Francis William** ⊕ South Bend, Wash.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1911; an Associate Fellow of the American Medical Association; an officer in the medical corps of the U. S. Army in France during World War I; medical examiner for the Selective Service during World War II; formerly associated with the U. S. Public Health Service; served as mayor of South Bend and as president of the Chamber of Commerce; died November 20, aged 73, of acute coronary disease.

**Barber, Walter M.,** Grove City, Pa.; Jefferson Medical College of Philadelphia, 1882; died November 12, aged 92, of influenza.

**Beck, Ralph Leslie,** Winfield, Texas; Fort Worth School of Medicine, Medical Department of Texas Christian University, 1917; died in Pittsburg, Texas, November 13, aged 61.

**Bennett, Frederick Sherwin,** Boston; Harvard Medical School, Boston, 1894; died November 20, aged 78.

⊕ Indicates Fellow of the American Medical Association.

**Benson, Oscar Gustav** ⊕ Plentywood, Mont.; Creighton University School of Medicine, Omaha, 1935; died December 14, aged 44, of cerebral hemorrhage, coronary occlusion and hypertension.

**Glasier, Mina B.,** Bloomington, Wis.; the Hahnemann Medical College and Hospital, Chicago, 1883; member of the American Medical Association; past president and for 35 years secretary of the Grant County Medical Society; president in 1935 and vice president in 1937 of the state board of health, of which she had been a member for 14 years; in 1932 received the Council Award of the State Medical Society of Wisconsin for meritorious service; died November 16, aged 91, of hypostatic pneumonia.

**Godfrey, George Butler** ⊕ St. Louis; St. Louis University School of Medicine, 1905; affiliated with Christian and Missouri Baptist hospitals; died in Jewish Hospital November 19, aged 72, of heart disease.

**Hendricks, Ralph** ⊕ Spokane, Wash.; University of Louisville (Ky.) Medical Department, 1906; an Associate Fellow of the American Medical Association; member of the American Public Health Association; served in France during World War I; for many years city health officer and city commissioner; died in Sacred Heart Hospital November 16, aged 80, of hemorrhage due to bishydroxycoumarin (dicumarol®) sensitivity.

**Jones, Fred Wade,** Tavernier, Fla.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; veteran of the Spanish-American War and World War I; member of the Illinois State Medical Society and American Academy of Ophthalmology and Otolaryngology; formerly practiced in Alton, Ill., where he was on the staff of St. Joseph's and Memorial hospitals; died November 16, aged 70, of carcinoma.

**Koeb, Roland Anthony,** St. Louis; St. Louis University School of Medicine, 1924; member of the American Medical Association; died in Barnes Hospital November 14, aged 52, of congestive heart failure.

**Kolski, John Joseph** ⊕ Pittsburgh; Medico-Chirurgical College of Philadelphia, 1911; member of the American Association of Industrial Physicians and Surgeons; on the staff of Southside Hospital; died November 19, aged 63, of cerebral hemorrhage.

**Le Kites, Delbert Lee P.,** Chincoteague Island, Va.; University of Louisville (Ky.) Medical Department, 1909; member of the American Medical Association; honored by the Veterans of Foreign Wars in Chincoteague Island with its civic award for outstanding community service; died November 2, aged 70, in an automobile accident.

**Lenont, Charles B.** ⊕ Virginia, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1899; fellow of the American College of Surgeons; served on the staff of Virginia Municipal Hospital; died November 5, aged 81, of lymphatic leukemia.

**Lewis, Loren E.,** Valparaiso, Ind.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1907; formerly county coroner; died November 11, aged 68, of heart disease.

**Malcolm, William Jackson,** Jericho, N. Y.; New York University Medical College, New York, 1898; member of the American Medical Association; past president of the Associated Physicians of Long Island; for many years school physician; died November 18, aged 83.

**Manley, Thomas Henry Jr.,** Tarentum, Pa.; University of Pittsburgh School of Medicine, 1910; member of the American Medical Association; found in the Allegheny River November 16, aged 63.

**Mathewson, Eugene,** Bostonia, Calif.; Gross Medical College, Denver, 1894; died in San Diego November 7, aged 90.

**Meek, Loring C.,** Tiosa, Ind.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1897; member of the American Medical Association; died November 8, aged 79, of cardiovascular renal disease and gangrene of the legs.

**Mendelsohn, Louis** ⊕ Saratoga, Calif.; Harvard Medical School, Boston, 1904; for many years affiliated with the Stanford University Hospital in San Francisco, where he died November 12, aged 71, of brain tumor.

**Miller, Charles Conrad,** Chicago; Hospital College of Medicine, Louisville, Ky., 1902; member of the American Medical Association; died November 25, aged 69, of coronary thrombosis.

**Monosson-Friedland, Ida,** Vineland, N. J.; University of Moscow Faculty of Medicine, Russia, 1922; member of the American Medical Association; died in Atlanta, Ga., November 11, aged 59.

**Moore, James Arthur** ⊕ Detroit; Meharry Medical College, Nashville, Tenn., 1899; died November 14, aged 75, of cerebral thrombosis.

**Moses, Joseph Snyder,** Freeport, N. Y.; University of Pennsylvania School of Medicine, Philadelphia, 1901; died recently, aged 72, of arteriosclerotic heart disease.

**Novak, Anthony Joseph,** McKeesport, Pa.; Georgetown University School of Medicine, Washington, D. C., 1934; interned at St. John's General Hospital in Pittsburgh; member of the American Medical Association; served as an officer in the medical corps of the U. S. Army in the Pacific theatre of operations during World War II; on the staff of McKeesport Hospital, where he died November 1, aged 43.

**O'Leary, Timothy James,** East Troy, Wis.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1903; member of the American Medical Association; affiliated with Burlington Memorial Hospital, Burlington, and Lakeland Hospital in Elkhorn; died in the Sacred Heart Sanatorium, Milwaukee, recently, aged 69, of heart disease and hypertension.

**Pearce, George Girdwood,** New Bedford, Mass.; Columbia University College of Physicians and Surgeons, New York, 1912; member of the American Medical Association; affiliated with St. Luke's Hospital, where he died November 6, aged 63, of coronary occlusion.

**Perrins, Harlan Bassett** ⊕ New Haven, Conn.; Yale University School of Medicine, New Haven, 1918; associate clinical professor of obstetrics and gynecology at his alma mater; specialist certified by the American Board of Obstetrics and Gynecology; served during World War I; fellow of the American College of Surgeons; affiliated with Grace-New Haven Community Hospital; consulting obstetrician and gynecologist to Griffin Hospital, Derby; died in Grace Hospital November 9, aged 56, of carcinoma.

**Reed, Roy Wentworth** ⊕ Richland, Mo.; University of Louisville (Ky.) School of Medicine, 1938; served in the Aleutian Islands during World War II; died November 10, aged 35, of cerebral hemorrhage.

**Reed, William Anderson** ⊕ Chattanooga, Tenn.; University of Tennessee Medical Department, Nashville, 1908; on the staff of the Erlanger Hospital, where he died November 11, aged 67, of coronary thrombosis.

**Reeves, Walter Bascum,** Greenville, Texas; St. Louis University School of Medicine, 1905; member of the American Medical Association; past president of the Hunt-Rockwall-Rains Counties Medical Society, Fourth District Medical Society, Texas Railway and Traumatic Surgical Association and the North Texas Medical Association; member of the Texas Public Health Association; vice president and a director of the Citizens' National Bank; died in Dallas October 1, aged 74, of ventricular tachycardia.

**Reising, Kenneth Christopher** ⊕ Louisville, Ky.; University of Louisville School of Medicine, 1932; on the active staffs of the Norton Memorial Infirmary, SS Mary and Elizabeth Hospital, Kentucky Baptist Hospital, Jewish Hospital and Red Cross Hospital; on the consulting staff, Kosair Crippled Children Hospital; on the courtesy staffs, St. Anthony's and Methodist Deaconess hospitals; died November 21, aged 43, of heart failure.

**Ripley, E. C.,** Decatur, Ga.; Atlanta Medical College, 1892; died in the Emory University (Ga.) Hospital October 25, aged 81, of pneumonia following an operation.

**Rogers, Vernon Stover,** San Antonio, Texas; University of Pennsylvania School of Medicine, Philadelphia, 1921; died November 1, aged 65, of coronary thrombosis.

**Ross, Samuel Boyd,** Philadelphia; Baltimore Medical College, 1912; served during World War I; died in Jefferson Hospital October 25, aged 69, of chronic myocarditis.

**Sands, Robert Lyman** ⊕ Santa Monica, Calif.; University of Nebraska College of Medicine, Omaha, 1919; served during World Wars I and II; died November 6, aged 54, of coronary occlusion and hypertension.

**Shepherd, Walton S.,** ⊕ Charleston, W. Va.; Medical College of Virginia, Richmond, 1900; fellow of the American College of Surgeons; since 1933 reviewing ophthalmologist to the Department of Public Assistance; owner of Shepherd's Eye, Ear, Nose and Throat Hospital; died November 11, aged 77, of carcinoma of the prostate.

**Shobe, Walter Rodes,** Indianapolis; Meharry Medical College, Nashville, Tenn., 1944; member of the American Medical Association and the Indiana State Medical Association; resident in obstetrics and gynecology at Kansas City General Hospital, Kansas City, Mo.; served during World War II; died November 8, aged 31.

**Shumway, John Nelson,** Painted Post, N. Y.; University of Buffalo School of Medicine, 1895; member of the American Medical Association; served as secretary of the Steuben County Health Officers' Association and as president of the Corning Academy of Medicine; for many years health officer; affiliated with the Corning (N. Y.) Hospital; died November 3, aged 88, of arteriosclerosis.

**Vallandingham, James Lewis,** Lexington, Ky.; Kentucky School of Medicine, Louisville, 1902; member of the American Medical Association; veteran of World War I; formerly representative for Fayette County to the state legislature; at one time superintendent of Eastern State Hospital; on the staffs of Good Samaritan and St. Joseph's hospitals; died November 9, aged 72, of coronary occlusion.

**Walker, Marie Winchell,** Los Angeles; the Hahnemann Medical Colllege and Hospital, Chicago, 1899; died November 11, aged 75.

**Wallace, Hugh Stanley** ⊕ Ingram, Pa.; Jefferson Medical College of Philadelphia, 1922; served on the staff of Presbyterian Hospital, Pittsburgh, where he died November 10, aged 54, of cerebral hemorrhage.

**Wikle, Jesse Ollie,** Madison, Ala.; Birmingham Medical College, 1915; member of the American Medical Association; past president of Madison County Medical Society; during World War II examining physician for Selective Service System in Madison County; died recently, aged 58.

**Yanofsky, Hyman,** Chicago; Chicago Medical School, 1920; member of the American Medical Association; died in the Garfield Park Community Hospital November 30, aged 62, of carcinoma of the sigmoid.

**Young, John Perry Jr.,** ⊕ North Charleston, S. C.; Medical College of the State of South Carolina, Charleston, 1933; on the staff of Baker Memorial Sanatorium, Charleston; died November 3, aged 45, of coronary thrombosis.

**Young, Marion Goldie Pitt,** Seattle; New York Medical College and Hospital for Women, Homeopathic, New York, 1916; died November 15, aged 81, of coronary occlusion.

# GOVERNMENT SERVICES

## PUBLIC HEALTH SERVICE

**Help in Developing Civil Defense Plans.**—The facilities of the Public Health Service have been offered to states and territories in developing medical civil defense plans. Surgeon General Leonard Scheele sent a letter to that effect to the health directors of the states and territories after publication of the booklet Health Services and Special Weapons Defense by the National Security Resources Board. Dr. Scheele called attention to the section that designates the 10 regional offices, for the time being, as centers for technical assistance to the states in formulating, revising and maintaining civil defense health service plans. Regional Offices are maintained in Boston, New York, Washington, D. C., Cleveland, Chicago, Kansas City, Dallas, Denver, Atlanta and San Francisco.

**Study of Hypertensive Cardiovascular Disease.**—A long term epidemiological study of arteriosclerotic and hypertensive cardiovascular disease is being conducted in Framingham, Mass., by the National Heart Institute of the Public Health Service with the Massachusetts State Department of Public Health and the town of Framingham. Plans for the study were endorsed in principle by the public health committee of the Massachusetts Medical Society. Approval was also given by the New England Heart Association and by the physicians of Framingham.

About 6,000 residents, selected at random, between the ages of 30 and 59 are to be examined for cardiovascular abnormalities or disease in a special clinic in charge of Dr. Thomas R. Dawber of the Public Health Service, who heads the study. The clinic staff does not provide treatment. This is a research study in which diagnostic information is furnished only to the personal physician of the person examined. When there are abnormal findings, the person is referred to his physician for interpretation of the findings and such treatment as the physician may deem desirable.

Focus of the survey are those persons found to be apparently free of cardiovascular disease at the time of their first examination. They will be reexamined bienially until a sizeable number have been found to have acquired the disease. At that time a search will be made of the data accumulated for the factors that influenced the development of disease in one group and not the other. The initial examinations to be given under the study will be completed early in 1952.

All medical planning for the survey in Framingham is being done in consultation with a Technical Advisory Committee of 11 physicians from the Boston area who are experts in the fields of cardiology and public health. The committee was appointed by Dr. Vlado A. Getting, state commissioner of public health. The committee proposed hypotheses as to suspected etiological factors for testing; it suggested specific items for examination and laboratory study, and it advised on criteria for evaluation of these items.

Planning for community participation, an important factor in the survey, began months before the clinical examinations. A study of the town led to the appointment by the town health officer of a 15 member executive committee for the study. The committee, with its six subcommittees, is representative of the various community groups.

The Framingham survey is limited to persons in the age group 30-59, in order to include those most likely to develop heart disease during the long term study and to permit adequate sampling.

**Training of Asiatic Health Officers.**—Three health officials of southern Asiatic countries have arrived in the United States for one year of advanced training. Two officials from the Thailand Ministry of Health are at the University of Minnesota under fellowship programs sponsored by the Economic Cooperation Administration and the government of Thailand. Dr. Thanong Viriyachati, health officer in Rajaburi Province for the Thailand Ministry of Public Health, is studying public health administration to prepare for a post as a regional health officer on his return to Thailand. Dr. Viriyachati received his medical degree from Chulalongkoon University in 1939 and his degree from the School of Hygiene and Public Health of the University of Medical Sciences, Bangkok, in 1950. Mr. Udom Kanishtharat, sanitary engineer in the Thailand Ministry of Public Health, is also studying public health and on his return will be chief of the division of sanitary engineering of the Ministry of Health.

Dr. Aryadasa Amarasinghe, Ceylon, is studying veterinary public health at the University of Minnesota under the Point Four Program. Dr. Amarasinghe is Veterinary Surgeon in charge of the program for eradication and control of animal diseases in the Province of Bondorowela. He received his degree of Veterinary Science (G.V.Sc.) from Bengal Veterinary College, Calcutta, in 1939.

**Model Milk Regulations.**—Almost 60,000,000 Americans are living in areas that have adopted the milk ordinance recommended by the Public Health Service, Surgeon General Leonard A. Scheele said in announcing publication of the list of cities using the ordinance. In 1,468 municipalities and 367 counties and sanitary districts, the ordinance is in effect. It is also in effect on a statewide basis in 11 states and the territories of Alaska and Hawaii. The total population of the areas concerned is 58,878,145. "The ordinance recommends but does not require pasteurization," he said. "However, I advise all consumers of raw milk to pasteurize it at home as a health precaution."

The milk ordinance is not a set of minimum standards. It is a set of model milk regulations prepared by the Public Health Service with the aid of a national advisory board of experts. Dr. Scheele said the ordinance was first introduced in 1923.

**Personal.**—Dr. Erval R. Coffey, an Assistant Surgeon General, has been assigned to Thailand under the Foreign Economic Assistance Act of 1950. He will head a division of public health, within the ECA's Special Technical and Economic Mission to Thailand, which is designed to aid in removing the massive barriers of poor health obstructing the country's economic production.——Dr. James M. Hundley, chief of the Nutrition Section of the National Institute for Arthritis and Metabolic Diseases, has been appointed consultant on nutrition in the Office of Health Resources of the National Security Resources Board.

## VETERANS ADMINISTRATION

**Admiral Boone Succeeds Dr. Magnuson.**—Vice Admiral Joel T. Boone (USN, retired) has been appointed Chief Medical Director of the Veterans Administration to succeed Dr. Paul B. Magnuson. Admiral Boone, who is 61 years of age, retired after a long and distinguished career in the Navy Medical Corps including service as personal physician to Presidents Harding, Coolidge and Hoover. His latest previous assignment on active duty was as chief of the Joint Plans and Action Division of the Defense Department's Office of Medical Services. Dr. Magnuson formerly was chairman of the Department of Bone and Joint Surgery at Northwestern University Medical School, Chicago, and recently became professor emeritus. He gave up his practice in Chicago in 1945 at the request of General Bradley, then the Veterans Administration Administrator, who asked him to help reorganize the medical department of the VA.

**Radioisotope Program.**—Following is an abstract of a report submitted by Dr. E. H. Cushing, assistant chief medical director, Research and Education Service of the Veterans Administration:

The radioisotope program of the Veterans Administration was initiated in 1947. At present radioisotopes are employed,

in research, diagnosis and treatment, in 14 VA hospitals, all closely associated with medical schools where radioisotopes are employed. Radioisotope laboratories and facilities are being included in the construction plans of 23 new VA hospitals, of which 18 will be completed by the end of fiscal year 1952. In the eastern third of the United States, VA hospitals having radioisotope programs have the advisory services of Dr. Shields Warren; in the central third, Dr. H. L. Friedell, and in the western third, Dr. Stafford Warren. A radioisotope committee, selected by the local Dean's Committee from the teaching staff of the associated universities, advises the local director of a radioisotope unit in respect to policies, personnel qualifications, professional and technical matters, human applications, radiological safety and public information. Usually five to eight persons are employed full time in a single unit. In addition, usually two or more persons from the faculty or laboratories of the associated medical schools serve on a part time basis, and still others serve as consultants. Not all units are, at this time, so completely staffed. The facilities of the radioisotope program include:

1. Administrative office.

2. Laboratories with specially constructed hoods, chemical benches, et cetera, fitted out with instruments and equipment.

3. Clinical room, where patients are brought for diagnostic studies. In a few instances, special beds have been set aside for these patients so they can be observed more advantageously. Expenditures to date total $1,625,682.

In research, two outstanding achievements of VA radioisotope units have been:

1. The development of a technic at VA's Hines Hospital, in connection with Northwestern Medical School, for using diiodofluorescein tagged with radioactive iodine for diagnosis and accurate location of brain tumors in 95 per cent of the more than 300 cases studied.

2. The development of a technic, at the Veterans Administration Center in Los Angeles in connection with the medical school of the University of California at Los Angeles, for making a thyroid function study employing only 1 microcurie of radioactive iodine and a scintillation counter. This test will probably replace the basal metabolism test in clinical practice. It is more accurate, is entirely safe and permits repeated tests.

In treatment, radioisotopes have been employed in polycythemia, leukemias, certain malignant diseases of the thyroid gland and selected cases of thyrotoxicosis. A conservative position is maintained.

Conferences are held once or twice a year, at which time progress is reported and problems of common interest are discussed. These are attended by a physician and a scientist from each of the 14 radioisotope units.

### CIVIL DEFENSE TRAINING

The Veterans Administration will accept responsibility for civil defense preparations within its own establishments, including training. A plan for training VA personnel in three different but closely related subjects has been drawn up, and the first phases of instruction have been initiated: (1) medical aspects of atomic warfare, (2) medical aspects of radiological defense and (3) radiological defense (monitors).

The laboratories and staff of specialists of the radioisotope units could render a most important community service in the event that an atomic attack produced a residual radiation hazard. One hundred and twenty-three or more "radef" teams dispersed in 14 widely scattered hospitals are available to the VA for such needs as it may have in connection with civil defense preparations within its own establishments. It is expected that four VA hospitals (Martinsburg, Hines, Houston and Long Beach) will be designated as VA "radef" training centers, to which personnel from VA hospitals not having radioisotope units may be sent to be trained to serve as monitors on VA "radef" teams.

**Disabled Korean Veterans and Public Laws 16 and 894.**—The Veterans Administration has issued regulations outlining conditions under which veterans, disabled after fighting started in Korea, may be entitled to rehabilitation training. The training, previously limited to World War II veterans, was extended to many veterans disabled on or after June 27, 1950, by Public Law 894, signed by the President late last year. Most of the policies and procedures set up under Public Law 16 itself have been carried over to the new training program. The newcomers apply for training on the same forms used by disabled World War II veterans.

Under Public Law 894, a veteran must have been disabled after the Korean conflict began and prior to a date yet to be fixed. The new law requires that the disability be such that VA may pay compensation at full wartime rates. Such rates are paid for disabilities or injuries resulting from armed conflict, or during extra-hazardous service, or while the United States is engaged in war. Under the new law, the July 25, 1956 deadline for Public Law 16 training will not apply to the newly disabled veterans. Instead, they will have nine years from the end of the current emergency in which to train.

Public Law 894 states that veterans who already had GI Bill or Public Law 16 training, as a result of their World War II service, may be entitled to additional training, if found necessary because of new disabilities. In determining whether such a World War II veteran needs training, and what type he should get, VA will consider his previous records of advisement and training as well as his current medical record. In the case of a veteran who interrupted Public Law 16 training to reenter the armed forces, VA also will evaluate his past training record and present medical file, to determine whether he still is able to proceed in the same employment objective.

**Personal.**—Dr. Alfred P. Upshur, manager of the Veterans Administration Hospital, Staten Island, N. Y., will become manager of the new 1,000 bed VA hospital at East Orange, N. J., which is scheduled to open next fall. Dr. Upshur served in the Regular Army Medical Corps for many years, then entered private practice in New York City. In 1941 he reentered the Army, serving as commanding officer of the La Garde General Hospital at New Orleans and of the Army-Navy General Hospital at New Orleans and of the Army-Navy General Hospital, Hot Springs, Ark. He was released from active duty as a colonel in 1946.

**Hospital News.**—Dr. William B. Terhune, associate clinical professor of psychiatry at Yale Medical School, New Haven, addressed the staff of the Veterans Administration Hospital, Northport, L. I., N. Y., January 11, on "Teaching the Technics of Personal Mental Hygiene as a Means of Helping the Neurotic Individual."

## MISCELLANEOUS

**Fellowships in Industrial Medicine.**—The U. S. Atomic Energy Commission will offer four fellowships in industrial medicine for the 1951-1952 academic year, continuing a special fellowship program begun last September. Fellows are selected by a committee headed by Dr. James H. Sterner, associate medical director of the Eastman Kodak Company and consultant in industrial health to the AEC.

The purpose of the special fellowship program is to provide advanced training and on-the-job experience to doctors in the field of industrial medicine, particularly in relation to the atomic energy industry. Awards are for one year's academic training at approved institutions of the fellow's own choosing. After completion of this training, fellows will be eligible to apply for a second year's inplant training at one of the major installations of the AEC. The stipend for the first year's training will be $3,600, plus tuition and laboratory fees, and for the second, or inplant, year, $5,000.

The fellowships are open to citizens of the United States who hold an M.D. degree from an approved medical school and who have had at least one year of internship. All fellows must be investigated by the FBI and cleared by the AEC for access to restricted data before entering on their fellowships. Applications should be submitted by March 1, 1951 to: AEC Fellowships in Industrial Medicine, Atomic Energy Project, School of Medicine and Dentistry, University of Rochester, Rochester, N. Y.

# FOREIGN LETTERS

## LONDON

**Doctors and the "Closed Shop."**—In 1946 the Willesden (London) Borough Council ordered that all its employees join a trade union. A famous dispute arose immediately, on the subject of the "closed shop." The Minister of Health at that time stated that, while he was anxious that doctors join a trade union, he considered that this matter should not be determined by the unilateral action of local authorities. The result was that the doctors won the fight.

At the annual representative meeting of the British Medical Association in 1947, it was declared to be undesirable in principle that any medical practitioner should be required to join any body, British Medical Association or other (excepting only a defense society), and that when any authority imposed such a requirement on its officers or candidates for office the British Medical Association should protest and afford financial help to any practitioners suffering as a result of having followed the association's advice.

The subject was reopened after a meeting of the Durham County Council on Nov. 1, 1950, when it was decided that all its staff should be members of an appropriate trade union. Nine days later a letter was sent by the county council to all its medical officers, nurses and teachers, requesting evidence of membership in such a trade union and stating that, if evidence of such membership were not furnished by November 22, the employee would be discharged but offered reemployment if he or she became a member of a trade union. In the case of doctors membership of the British Medical Association would meet the requirements.

On November 15 news of the issue of this letter was received by the British Medical Association; the secretary of the association immediately sent a letter to every medical officer employed by the Durham County Council, reminding them of the association's opposition to the "closed shop." The letter invited the medical officers concerned to postpone action on the county council's directive until after a meeting of medical officers on November 18 at Bishop Auckland General Hospital.

### DR. CHARLES HILL IN PARLIAMENT

On the same evening (November 15) Dr. Charles Hill, member of Parliament, drew the attention of the House of Commons to this matter. It seemed to him that the requirement of the Durham County Council that every member of its staff produce evidence of trade union membership, under threat of dismissal, was wrong in several respects. To secure membership under duress was to damage the organization that secured it. Any organization or body from which a member who was dissatisfied with its officers or its policy or its work could not resign voluntarily without losing his job was an unhealthy one. The duty of a local authority was to employ the best qualified person to do its work, whether or not he belongs to this or that organization. The loss of membership for some offense within a trade union would involve the loss of the man's job.

He pointed out that the British Medical Association was a voluntary body. The Durham County Council had ordered the doctors to join either a trade union or the British Medical Association as they chose, but the attitude of the British Medical Association was that no doctor should be forced to join any body, even the British Medical Association. He was asked whether he knew of any doctors who had dared not to join the British Medical Association, and he replied that the membership was between 75 and 80 per cent of the profession, and that there was no compulsion with respect to joining. He thought that the nation was losing its capacity for anger at such interference with the freedom of the individual. He agreed that the battle for the right of association had been magnificent and necessary, and as one who had spent many years in collective bargaining he desired men and women to belong to their appropriate professional associations, but it seemed to him utterly wrong that a local authority should adopt the attitude of the Durham County Council. He hoped the Minister would take action as he had done in the Willesden incident.

Mr. E. R. Bowen, M.P., said that in December 1946 the Minister of Labour had said that compulsion by employers to join trade unions was likely to be detrimental to harmonious industrial relations. Over half the working population of the country were not members of trade unions affiliated with the Trade Union Council. That indicated the proportion of the population that might be affected by such actions as that of the Durham County Council.

Mr. Gordon Lang, M.P., said that, if it was to become a feature of public administrative life that a local governing body could order one to join a trade union, he could conceive of occasions when there might be an instruction that no employees of certain bodies were to belong to any trade union. He maintained it was not the duty of a local body to impose its will in that way on its employees. He believed that liberty was dwindling in this land, and he regretted it.

Mr. A. Blenkinsop replied for the Ministry of Health. He said the Ministry regretted the resolution passed by the Durham County Council. He said that in January 1948 the Minister of Health had hoped that persons employed in the National Health Service would be encouraged to belong to their appropriate organizations, but it would not be a condition of their employment and there would be no pressure on anyone to belong to any organization whether professional or trade union. The same view had been expressed by the Minister of Labour. He said it should be remembered that the Ministry was concerned merely with advising local authorities on matters of this kind and would call their attention to previous circulars. The only attitude that the Ministry could take up was one of adviser to the local authority on this point, and he pointed out that the county council was a locally elected authority with full power in the matter.

### THE TRADE UNION BILL

On Nov. 17, 1950, Mr. Nigel Davies, M.P., who had been successful in the ballot for private members' bills, introduced the Trade Union Bill, "to prohibit local and other public authorities from making membership or nonmembership of a trade union a condition of employment or of continuance in employment." Its second reading was set down for April 6, 1951.

### PUBLIC HEALTH COMMITTEE

A special meeting of the Public Health Committee of the British Medical Association, reported in the *British Medical Journal* of Nov. 25, 1950, was held on November 16 under the chairmanship of Dr. Metcalfe Brown, to discuss the situation in Durham following the resolution of the county council requiring all members of the staff to be members of an appropriate trade union. It was reported that the clerk of the Durham County Council had been informed of the policy of the association and the county council had been asked to receive a deputation and, in the meantime, to withdraw its requirements. It was agreed unanimously that the action of the Durham County Council was greatly to be deprecated.

The meeting at Durham on November 18 was attended by 36 medical officers who were employed by the Durham County Council. Letters of support were received from five medical officers who were unavoidably absent. Of the remaining 12 medical officers who were employed by the council, two were known to be hospitalized and one was on holiday. The chair was taken by Dr. G. Fenwick Lishman, immediate past president of the North of England Branch of the British Medical Association. Dr. Metcalfe Brown, chairman of the Public

The items in these letters are contributed by regular correspondents in the various foreign countries.

Health Committee, addressed the meeting. He pointed out that he was speaking as a member of the Council of the British Medical Association and the council of the Society of Medical Officers of Health and as a trustee of the British Medical Guild. He said the "closed shop" issue affected the whole of the profession. The British Medical Association was resolutely opposed to any requirement by an employing authority that medical practitioners be obliged to join any trade union or professional organization. It was totally irrelevant, he said, that the British Medical Association was acceptable to the Durham County Council as a union. The British Medical Association was naturally anxious to include as many doctors as possible within its membership, but it was absolutely opposed to any acquisition of members by coercion. The resolution of the Durham County Council was an intolerable interference with the private affairs of individual doctors. The medical profession was united in its opposition to this policy, and the Durham medical officers could count on the support of the British Medical Guild, which was backed by ample funds. The Medical Women's Federation whole heartedly supported the policy of the British Medical Association and had sent a letter to its members. He believed that the Royal College of Nursing, Royal College of Midwives and National Union of Teachers were also determined to oppose the county council's decision. The government position had been made clear in the House of Commons, where the Parliamentary Secretary of the Ministry of Health had stated that the government regretted the action taken by the Durham County Council. Dr. Metcalfe Brown concluded by advising the medical officers to ignore the county council's letter of November 10.

#### MUTUAL PROTECTION

A speaker at the same meeting pointed out that these events emphasized the need for medical officers to stand together for mutual protection. He had felt in the past that the British Medical Association was concerned only with the interests of general practitioners, and he was delighted to find that the association was prepared to take such energetic action on behalf of members of the public health service. It was totally unreasonable of the county council to demand that medical officers comply with their request within 12 days or be dismissed.

Another speaker inquired about the position of holders of combined appointments, that is county district medical officer of health and assistant county medical officer of health. Dr. Metcalfe Brown said that termination of these appointments would involve the consent of the Minister of Health.

#### COLLECTIVE AGREEMENT HONORED

Dr. E. Grey Turner, assistant secretary of the British Medical Association stated that the county council need have no fears about collective agreements. The British Medical Association would continue, as in the past, to negotiate collective agreements on behalf of the medical profession. Any agreements reached would continue, as in the past, to be honored by the whole profession. He had never understood the arguments sometimes put forth by advocates of the "closed shop" to the effect that union members could not bear to work alongside nonunion men. In his experience the doctors working in a hospital would never dream of inquiring which of their colleagues were members of the British Medical Association or any other professional organization, let alone object to any who were nonmembers. All that mattered was that the doctors should give good service to their patients and to the public, and there was no reason to suppose that a doctor would give less good service to his patients because he happened not to be a member of the British Medical Association or any other organization.

#### COUNTY COUNCIL INSTRUCTIONS IGNORED

The meeting resolved by unanimous vote to ignore the county council's instructions and to affirm its whole hearted support to the policy of the British Medical Association with respect to the "closed shop." Dr. Lishman concluded the meeting by expressing his thanks to the speakers and said that he had never presided over a meeting in which the unanimity of feeling was more clearly obvious.

#### COUNTY COUNCIL DECISION REAFFIRMED

The lay press announced that on November 28 the Durham County Council had reaffirmed its decision to dismiss any of its employees who did not provide evidence of membership of a trade union or professional association. As reported in the *British Medical Journal* of Dec. 9, 1950, at a second meeting of medical officers employed by the county council on December 2 in Durham, 39 medical officers attended and five others sent letters of support. Dr. William Hunter, secretary of the North of England Branch of the British Medical Association, took the chair. The meeting was addressed by Dr. E. Grey Turner, assistant secretary. Dr. Grey Turner said he had read in the press an argument put forward by the county council in support of its "closed shop" policy, namely, that nonmembers of unions or associations should not enjoy the benefits of terms and conditions of work negotiated by the unions or associations. The British Medical Association, on the other hand, was content that the small minority of nonmembers should enjoy the fruits of its labors on behalf of the medical profession. Any nonmember could walk into British Medical Association House, London, and receive expert advice and help without hindrance or charge. The association was convinced that an open-handed and generous attitude to nonmembers was far the best way of persuading them to become members. Dr. Grey Turner gave further evidence of united support from the medical profession in opposition to the "closed shop" policy and called on Durham medical officers to continue their resistance to the council's instructions. At the end of the meeting arrangements were planned by which the work of any doctor dismissed would not be undertaken by any other doctor. There was a unanimous resolve by the meeting to adhere to its earlier decision to ignore the instructions of the county council.

## PARIS

**Paraoxypropiophenone, a Powerful Synthetic Hypophysial Inhibitor.**—Paraoxypropiophenone (H 365) is the first practical achievement of a new system of chemotherapy perfected by Professor Buu-Hoi in the laboratories of the Radium Institute. Its formula is similar to that of diethylstilbestrol. Its action is basically the same as that of natural or synthetic estrogens, but it has the advantage that it lacks their peripheral effects, being practically devoid of estrogenic potency. It inhibits pituitary production of gonadotropin and thyrotropin but does not influence the production of corticotropin. It was first tried by Perrault, Vignalou and their associates, with variable success in the sudden flushes of the menopause.

Next, using as their rationale the functional parallelism between the placenta and the hypophysis, they used paraoxypropiophenone alone in a patient with malignant chorioepithelioma with pulmonary metastasis. Six months later the patient was apparently clinically, biologically and radiologically cured, and there was no recurrence 18 months after the beginning of the treatment and eight months after its cessation. In three other moribund patients, evolution was only delayed. Professors Lacassagne and Hinglais are also treating a series of patients with paraoxypropiophenone, with encouraging results. As stressed by Latarget, a wider experience is necessary, which is difficult because of the rarity of chorioepithelioma. In other cancers uncertain results were noted. Perrault stresses that this drug has no direct cellular effect and can act only by hypophysial inhibition. Since 1949 the authors have treated more than 300 patients with partial or total hyperfunction of the hypophysis or of the diencephalohypophysial unit.

In toxic diffuse goiter (Basedow's disease) the authors obtained favorable and sometimes spectacular results, especially in cases with a strong hypophysial predominance. Regression of exophthalmos occurred within three weeks. They believe that paraoxypropiophenone will be the drug of choice in the treatment of this disease. Adjunct treatment (such as with thyroxin or sedatives) may be necessary in the beginning but becomes unnecessary as soon as hormonal balance is

restored. In one patient a hyperthyroid crisis, precipitated by breast feeding, was brought under control within 36 hours without interruption of lactation. On July 7, 1950, Professor de Gennes and his associates reported, at a meeting of the Medical Society of the Paris Hospitals, successful results in a case of malignant exophthalmos. Among others, P. Guinet (Lyons) and J. Mahaut (Brussels) confirmed the remarkable action of this drug. The use of paraoxypropiophenone is indicated in syndromes characterized by hyperproduction of thyrotropin and, sometimes, hypothyroidism following a too extensive thyroidectomy or the administration of too large doses of synthetic antithyroid agents. The drug prevents the goitrogenous action of thiouracil in experimental animals.

Results with the drug in cases of overproduction of gonadotropin A are good, especially in Gilbert Dreyfus' hyperfolliculinic syndromes, Seguy's estrogenic disease and Ferrier's hypophyso-ovarian dysfunction. In two cases of Rhiel's melanosis Perrault and his associates obtained success in one and failure, owing to too small a dose, in the other. On June 8, 1950, at a meeting of the Society of Dermatology and Syphilology, Grupper and his associates reported on five cases of facial melanosis treated successfully with H 365. The dose was 1 to 2 Gm. given daily for four to six weeks. They believe that this compound may inhibit the synthesis of melanosis by blocking tyrosinase. The drug appears to have been effective in some cases of diabetes mellitus, arthritis and obesity. Treatment with the drug does not seem to be indicated in syndromes due to overproduction of pituitary adrenocorticotropic hormones (e. g., Cushing's syndrome).

The recommended dose is 0.05 to 0.30 Gm. per day in mild cases and as a maintenance dose and 0.25 to 1.5 Gm. per day or more in severe cases. The material can be given in suppository form. Without interruption of therapy during the menses, hormonal balance is obtainable within three months: thereafter it should remain stable for three to four months. The drug is nontoxic; 0.4 Gm. per day provokes no toxic signs in mice. No blood, renal or hepatic damage is produced in man. In five cases (less than 2 per cent) M. Perrault and his associates observed a transient gastrointestinal intolerance, which could be avoided by administration of the drug during meals. Six cases of pseudopregnancy were observed and corrected by discontinuance of treatment for seven to 10 days or by use of a smaller dose. In some patients (obese women) significant retention of water was corrected by therapy. Peripheral estrogenic effects were not observed, either in male or female patients, even after the administration of large doses. Paraoxypropiophenone is not an abortifacient; on the contrary, in certain cases it appeared to increase fertility and prevent abortion.

**Streptomycin in Genital Tuberculosis of the Female.**—L. Masse, Demade and their associates reported, at a meeting of the National Academy of Surgery, encouraging results of streptomycin therapy in gynecologic cases. In six female patients the diagnosis of genital tuberculosis was confirmed by a laboratory examination, and in three cases it was based on characteristic clinical signs. Results were successful in three cases of metroadnexitis, three of fistulous pelviperitonitis, and two of pyosalpynx. Treatment failed in a seriously ill pregnant patient with tuberculous adnexitis. Treatment was begun with a daily dose of 1 to 2 Gm. and regulated according to the blood concentration of the antibiotic. In cases with diminished renal function due to associated renal tuberculosis, a satisfactory blood concentration was obtained with small doses of streptomycin. In cases with fistulas, the authors injected 100 mg. of streptomycin into the fistulous passage. In gynecologic as in other diseases, results are best in acute or subacute cases. Also, with the aid of streptomycin therapy, patients who were formerly deemed inoperable, because of the advanced stage of their disease, can be well prepared for operation. These good results, obtained one year and a half ago, seem permanent, but it is still too early to permit definite conclusions.

**Streptomycin in Tuberculosis of the Aged.**—At the meeting of the National Academy of Medicine on July 4, 1950, Ch. Mattei reported on streptomycin therapy in tuberculosis in old persons. In a group of 12 patients from 60 to 78 years of age, he obtained excellent results, confirmed by projected radiographs. A 68 year old woman was successfully treated for severe generalized miliary tuberculosis with 250 Gm. of the drug. In a 60 year old patient with tuberculous cystitis and renal and pulmonary tuberculosis, 240 Gm. of streptomycin and 15,000,000 units of penicillin effected the disappearance of bacilluria and renal signs and remarkable clearance of pulmonary fields. Two patients, 60 and 63 years old, were rapidly cured of serofibrinous pleurisy with 80 and 100 Gm. of the antibiotic. In two febrile patients (aged 60 and 78) with pulmonary cavitation 200 to 300 Gm. of streptomycin rapidly produced apyrexia and cleared the pulmonic lesions. In 67 year old patient, with a lobite, one treatment with 200 Gm. of the antibiotic cleared the pulmonary fields. A cavity persisted, necessitating repeated pleuroscopy, but section of adhesions and faradization were performed without untoward results. His condition is now excellent. As a rule the dose was 2 Gm. per day administered in five or six intramuscular injections. The author stressed that streptomycin therapy should be as intensive in old persons as in patients under 50 years of age. Prof. A. Lemierre confirmed these observations in a 73 year old patient with severe pulmonary tuberculosis, which rapidly improved with streptomycin therapy.

## ITALY

**Ultrasonics in Therapy.**—At the International Medical Meetings of Verona the subject of ultrasonics was discussed by Professor Ponzio, director of the Institute of Radiology of the University of Turin, Professor Villa, clinician of the University of Milan and Fanucchi, associate professor at the medical clinic of the University of Milan. Professor Ponzio recalled that the first notion of the existence of ultrasonic waves, the study of their physical and biologic properties and the research concerning their use go back about 50 years. In the last 20 years investigations have been rather numerous and clinical experience has been acquired with ultrasonic waves, using mainly devices with a piezoelectric quartz base. The instruments used at present generate sound waves having a frequency of 500,000 to 1,000,000 or more vibrations per second.

Any substance, solid, liquid or gaseous, when exposed to ultrasonic action undergoes transitory or permanent disturbances of structure, variable in form and degree. Liquids, especially, undergo violent vibrations and shaking up. Among other effects are overheating by friction and the important phenomenon of cavitation, the formation of small bubbles of gas in the liquid. Many cell changes are attributed, in biology, to this phenomenon. Transformations of the chemical state may be produced in substances exposed to ultrasonic energy, such as flocculation in colloidal substances, and phenomena of oxidation, polymerization and coalescence. Systematic studies of the biologic action of ultrasonic waves have shown that the mechanism of action is manifold and varies according to the organism. It is possible to cause direct changes in bacteria and other unicellular organisms simply by a definite increase in the frequency of the waves. Recently (1950), complete destruction of cultures of bacilli was obtained. Definite conclusions cannot yet be drawn from research done on viruses and their vaccines, although this work is of much interest. Effective vaccines were obtained recently from cultures of Streptococcus and of typhus and pertussis organisms in which the immunizing power appeared superior to those of vaccines obtained by the usual methods. The behavior of micro-organisms, suspended in liquid exposed to pressure by currents of ultrasonic waves, is also of great interest. Microscopic observations revealed that the infusoria may be reduced to fragments by crushing, and analogous destruction can be observed in blood cells suspended in plasma.

In protoplasm exposed to pressure by ultrasonic waves, profound structural changes have been observed as a result of whirlpool movements and cavitation. However, great plasticity of the cell elements was observed. Experimental observations of the action of ultrasonic waves on multicellular organisms and on their complex tissues have provided evidence of phe-

nomena similar to but more complex than those undergone by unicellular organisms. Recent microscopic investigations at the Radiological Institute of the University of Turin have revealed that, in the higher animals, the striate and the cardiac muscles are more affected by ultrasonic waves than are the viscera. High ultrasonic intensity may produce laceration, dissociation and fragmentation of the muscles.

Professor Villa emphasized the fact that the application of ultrasonic waves in therapy—although derived from biologic research on ultrasonics—has developed in a completely different direction. It has been thought that while high ultrasonic intensities cause cellular destruction and the medium range intensities cause phenomena of inhibition, those in a limited range may produce beneficial stimulation of the metabolism of tissues. On the basis of the more recent literature, the speaker mentioned the various diseases treated with ultrasonics, especially neuralgia, vertebral myalgia, arthropathy—especially of the degenerative type, suppurative processes of the skin and subcutaneous tissue, ulcerative cutaneous lesions and diseases of the peripheral vascular system. In these diseases, ultrasonic therapy frequently was effective, but also had failed many times.

Professor Fanucchi discussed chiefly the results obtained at the Medical Clinic of the University of Milan with about 100 patients, who submitted to ultrasonic therapy from 1948 to 1950. Favorable results were obtained especially in recent cases of primary sciatica, in lumbar arthrosis and in pain caused by neurinomas in amputation stumps. Good results were also obtained in neuralgic processes or in sciatica associated with ankylosing spondylitis. The speakers stressed the fact that definite favorable conclusions cannot be drawn concerning the effects of ultrasonic therapy on inflammatory and degenerative lesions of the joints. With respect to technic of application, the speakers concluded from their personal experience that ultrasonic massage is particularly indicated in those cases in which the pain is diffuse, while the application of a focused ultrasonic beam is preferable when the pain is well localized.

It was concluded that ultrasonic therapy is still in a developmental stage and that caution is indicated until further experiences confirm its usefulness. This attitude, although reserved, is not skeptical.

## SWEDEN

**The Codex Ethicus and the World Medical Association.**—The annual meeting of the World Medical Association to be held in Stockholm in September 1951, over which Dr. Dag Knutson, publisher of *Svenska Läkartidningen,* and president of the Swedish Medical Association, will preside, is already receiving careful thought and discussion in the Swedish medical world. The subject was debated at a meeting of the Swedish Medical Association last August, and much of what was said on this occasion has been published in successive numbers of *Svenska Läkartidningen,* the organ of the Swedish Medical Association. In the Nov. 17, 1950 issue of this journal, Dr. Walo von Greyerz of Stockholm answers emphatically in the affirmative his own question: Is an international medical association needed? In his opinion, the World Medical Association already justified its existence and hopes for the future. Its greatest value may depend on its existence as a forum before which doctors throughout the world can give expression to their views on factors and reforms affecting the world's health. The World Medical Association enables strong countries to help the weak and facilitates the exchange of useful information throughout the world. Sweden already has a well organized medical service, and the World Medical Association offers Sweden a welcome opportunity to help other countries less well equipped in this particular respect.

With regard to the drafting of a new Codex Ethicus to serve as a guide to the conduct of medical practitioners, Dr. Dag Knutson has pointed out that such a code may be more needed now, with so much that is new and in the melting pot, than was the case some time ago. He would like to see such traditions put down clearly on paper, rather as the enunciation of general principles than as an attempt to go elaborately into details. It is surely unnecessary to give Sweden an ethical code so bulky that it has the effect of a lexicon. Dr. Sten von Stapelmohr is also in favor of drawing up a new ethical code. As he points out, the past half-century has witnessed an enormous change in the conditions under which medicine is practiced in Sweden. In 1900 there were only 1,131 doctors in Sweden, while in 1949 there were 4,548. Their numbers have been more than doubled since 1926. Only 20 years ago the population of Sweden was quite homogeneous, nurtured in the same peaceful traditions and speaking the same language. Now it has been invaded by thousands of refugees from abroad, and more than 300 foreign doctors have joined the Swedish medical profession. Under these conditions it would be salutary to possess a generally accepted ethical code, to be mastered by all and appealed to by all in case of need. In such a perplexing problem as that of bacterial warfare, for example, it may be difficult to distinguish clearly between the claims of the state and the moral claims of the individual. The draft of a new Codex Ethicus presented by the Central Committee of the Swedish Medical Association for discussion by its members runs, on the whole, on the lines of the international code of medical ethics adopted by the World Medical Association in 1949.

## BELGIUM

**Idiopathic Steatorrhea.**—At a special session of the Belgian Society of Gastroenterology, the subject of idiopathic steatorrhea was studied by several authors. Dumont-Ruyters showed that idiopathic steatorrhea is clinically indistinguishable from other digestive diseases, especially in certain disturbances of hepatopancreatic secretion. Clinically it is similar to the conditions termed tropical sprue, nontropical sprue and celiac disease. The disease has a variable symptom complex, made up of the association of a series of more or less complete deficiencies of absorption. Biochemically it is essentially a disturbance of assimilation of fats, the emulsion and splitting of which seem normal. According to recent studies of Frazer and collaborators, the condition constitutes an obstacle to the absorption of fat particles. Some of the other insufficiencies of absorption depend directly on the disturbance of the absorption of fats; others seem independent of this factor. The pathogenesis of the disease is still undetermined. There is no proof that it is based on a specific functional defect of the intestinal mucosa. It is possible that a factor necessary to its function is destroyed in the intestine. The causative factors are intestinal bacterial pullulation and dietary factors, especially the nature of the fats in the diet. Dr. Froelich, who summarized the discussions, said that the study of sprue is of interest because it is often unrecognized.

The discussion of the mechanism which conditions the impairment of fat absorption is centered on the problem of absorption of particles of neutral fats. Concerning the process itself, one has to rely on hypotheses. The septic nature of the contents of the small intestine may play an important role, as shown by the gastrojejunocolic fistulas. The presence of mucus in abnormal quantity may prevent the absorption of fats. Finally, the possibility of an alteration of the parietal phase must be considered. Future research will undoubtedly show that diverse processes play a part in the pathogenesis of sprue.

**Prof. Jean Verhoogen.**—Professor Verhoogen, who presided over the International Congress of Surgery in New Orleans, died recently, at the age of 86 years, in Brussels. He was professor at the Surgical Clinic at the University of Brussels from 1911 to the time of his death. He was one of the founders of the Belgian Society of Surgery and of the International Society of Surgery, of which he had been president since 1929.

The scientific work of Jean Verhoogen was of great importance. Numerous reports on general surgery and urology demonstrate his active hospital career, especially between the years 1888 and 1929.

# CORRESPONDENCE

## INFLUENZA EPIDEMIC IN GREAT BRITAIN AND EUROPE

**To the Editor:**—In response to your request of January 15, the following information is offered concerning the current influenza situation in this country, in England and in Continental Europe.

The Influenza Information Center of the World Health Organization Influenza Study Program located at the National Institutes of Health of the Public Health Service in Bethesda, Md., has been receiving official and unofficial reports concerning the prevalence of influenza throughout the world for the past three years. These reports correlated with the information obtained by the National Office of Vital Statistics of the Public Health Service, and those of particular significance are published in the *Weekly Communicable Disease Summary*, which is sent to all public health officials and others interested.

On the European Continent a local outbreak in Sweden was reported in June 1950 and A′ virus was isolated in acute cases. According to incomplete reports in November localized cases appeared in Denmark and in northern Sweden and in Norway; they were more generally distributed in Sweden in December. A high incidence, involving 50 to 75 per cent of the population occurred in Godthaar, Greenland, in December, but the disease was not severe. Late in December influenza began to make its appearance in north England, particularly around Newcastle, which serologically was shown to be type A. Soon an unusual incidence was noted in Liverpool. The cases were in general mild, with fever lasting only three or four days. Early in January cases became more frequent in the Liverpool area and an increase in the number of deaths from influenza was noted in the reports. During the first two weeks of January other countries, including the Netherlands, Belgium, the British zone in Germany and northern Spain, reported an unusual number of influenza cases, though not of a severe type.

At this writing (January 24) in England the disease is still more or less confined to the northern area, centering about the Liverpool region, and there is not an unusually high incidence in London and the southern part of England. Influenza morbidity is not reportable, but the number of insurance claims for illness has given a good index of the amount of the disease in the general population. While deaths ascribed to influenza during an outbreak may be misleading, the number of deaths as reported due to influenza has increased in 126 great towns in England having a combined population of about 20,000,000. In the week ending January 13 there were 890 deaths—an increase of 432 over the previous week—reported as due to influenza. Eighty-five per cent of these deaths are of patients over the age of 55, which is in contrast to the experience during the 1918 outbreak, when there was an unusually high death rate in the young adult age group. Influenza A′ virus has been isolated in cases occurring in London, but details of the virus prevalent in Liverpool have not been received. This virus has also been isolated in Edinburgh and in Glasgow, but the disease is not epidemic in Scotland.

The Strain Study Center of the Influenza Study Program in the United States located at the laboratory of Dr. T. P. Magill, State University Medical Center, Brooklyn, and the National Institutes of Health laboratories at Bethesda have received a strain isolated from pooled throat washings in three cases in London. Dr. Magill has also received a strain isolated in Sweden and one isolated in Leiden, Holland. These appear to be A′ and are being studied for their antigenic characteristics.

A number of cases have been reported widely in the press as occurring on ships coming to this country from England. Nearly all of the patients had recovered on arrival in the United States, but attempts were made by two laboratories participating in the Influenza Study Program to isolate virus from crew members still ill on arrival.

A regular meeting of the Advisory Committee and Directors of Regional Laboratories of the Influenza Study Program [1] was held on January 18 in Bethesda. The situation was reviewed, and recommendations concerning vaccination were discussed. The participants agreed that the question of immunization against this outbreak or any outbreak is not settled, as there is no vaccine that can be expected to protect with certainty. However, the situation indicates the necessity for continuing controlled studies of the efficacy of influenza vaccines in man. Since the greatest part of the mortality results from bacterial complications in the respiratory tract, they felt that patients who have a severe influenza-like illness should receive appropriate antibiotics or chemotherapeutic agents. They pointed out that it is to be expected that some influenza will appear in the United States which will probably resemble the recent experiences with this disease. Many localized outbreaks of influenza A and A′ occurred in the United States last year.

In summary, a mild form of influenza seems to be widely prevalent throughout England and Continental Europe, from which A′ virus has been recovered. In the Liverpool area the disease appears to have its greatest concentration and highest mortality, which is, however, confined to the older age groups. Morbidity of the disease in the United States at this time is below the usual expectancy. From the above information it would seem reasonable to believe that an unduly severe outbreak of influenza this season is unlikely in this country.

LEONARD A. SCHEELE, M.D., Surgeon General,
Federal Security Agency,
Public Health Service,
Washington 25, D. C.

1. Advisory Committee: Dr. Norman Topping, associate director, National Institutes of Health; Capt. R. W. Babione, Office of Surgeon General, U. S. Navy; Major L. C. Kossuth, Office of Surgeon General, Department of Air Force, and Col. Don Longfellow, Office of Surgeon General, Department of Army. Directors of Regional Laboratories: Dr. Maxwell Finland, Boston City Hospital; Dr. Irving Gordon, New York State Health Department; Dr. A. P. McKee, University of Iowa; Dr. E. H. Lennette, California State Department of Health; Dr. M. Schaeffer, United States Public Health Service Virus Laboratory, Montgomery, Ala.; Dr. Jonas Falk, University of Pittsburgh, and Dr. T. Francis Jr., University of Michigan.

## THE BEDPAN

*To the Editor:*—The paper by Benton, Brown and Rusk on the bedpan and the bedside commode (*J. A. M. A.* 144:1443 [Dec. 23] 1950) offers experimental support to the practical observation that the bedpan, except in rare instances, is an antiquated and dangerous apparatus. May I recount the approach to the problem in Sweden, where I visited in 1949. The following paragraph is taken from a diary written at the time.

"Bedpans are rarely used, and then only for those persons who cannot sit on them. This reads as a paradox, but the Swedes have acknowledged, what every observer knows, that there is a greater strain on the organism, both psychic and physical, in using a bedpan than in sitting on a regular toilet. Accordingly, in the Södersjukhus (Southern Hospital, Stockholm), a device has been long employed which was reported from England in *The Lancet* a year or two ago. The money for this device was obtained from the municipal authorities only by pointing out that the psychic handicap to using a bedpan in the presence, seen or unseen, of others would encourage constipation, thus handicapping recovery and the freeing of the hospital bed for someone also in need of hospitalization. The device is a wheelchair with a toilet seat in place of the regular seat, and at a height sufficient to clear the top of the toilet bowl. The patient is either wheeled to the toilet room in this chair and then into a cubicle, or, if that would be too long a ride (as far as his physical forces, not the time, were concerned), his bed is wheeled into an anteroom of the toilet room where he is then placed on the unique wheel chair. As has also been the experience in England, the patients have been loud in praise of it. Anyone who has experienced the bedpan episode and then uses the device refuses to return to the former."

S. M. RABSON, M.D.,
St. Joseph Hospital, Fort Wayne 2, Ind.

# MEDICAL MOTION PICTURES

**Nutritional Aspects of Tropical Disease:** 16 mm., color, sound, showing time 30 minutes. Produced in 1950 by and procurable from E. R. Squibb & Sons, 745 Fifth Avenue, New York, or from Squibb field representatives and branch offices.

This is a report type of film describing the hospitalization of a group of seven patients suffering from one or more deficiency diseases, in most cases accompanied by parasitic infestation. The film is divided into three sections. The first, entitled "Upon Admission to the Hospital," describes the case histories of these patients, including their diets and symptoms of such nutritional deficiency diseases as beri-beri, macrocytic anemia of pregnancy, tropical sprue, pernicious anemia with subacute combined system disease, pellagra and extreme protein deficiency. The second section, entitled "Therapeutic Measures," discusses essentials of treatment in cases of nutritive failure. For each of the patients, individualized treatment, including administration of vitamin $B_{12}$, is demonstrated. After treatment, there is a disappearance of symptoms, restoration of appetite, improvement in weight and strength and cessation of diarrhea. In the last section of the film, the patients are shown prior to their discharge. Blood value charts and plasma protein determinations for each patient prior to, during and after treatment are shown. The importance of a healthful diet is emphasized.

The severe nutritional deficiencies illustrated in this film are rarely seen in the United States. The physician aspirated 5 cc. of bone marrow for the sternal puncture instead of 1 cc. or less, as is good procedure. The specific locale of the picture should be mentioned instead of "the tropics." The presentation of the history, diagnosis and treatment in one case at a time, instead of history and physical examinations for all seven and then treatment in each, would have been less confusing. The average person may not remember the patients in the proper order, since there is a great deal of similarity in the cases. There is too much repetition. It is most valuable for medical students to see these extreme forms. The film would be especially good for medical groups in South American countries. Although the film lacks continuity, the splendid clinical pictures make it worth seeing.

**Your Friend, the Doctor:** 16 mm., color, sound, showing time 11 minutes. Prepared by Fred V. Hein, Ph.D., and Donald A. Dukelow, M.D., Bureau of Health Education, American Medical Association. Produced in 1950 by and procurable from Coronet Films, 65 East South-Water Street, Chicago 1.

This is the story of the relation of 11 year old Jimmy and his family with their doctor. Jimmy's family has moved to a new home. Early in his experience in his new school, Jimmy meets the public health nurse serving the school and learns from her that a school health appraisal is necessary. On taking certain notices and a card to be filled out to his mother, he finds that this is an activity of interest to the whole family. In the family conference, Jimmy learns that his family has already selected a family physician and sees the name, Albert V. Evans, M.D., on the family telephone list. On the day that Jimmy returns his card to the school nurse, he finds out how important the information on the card is to the nurse. His friend Howard has been hurt, and the nurse, by referring to the card, finds his mother's telephone number; when she calls but gets no answer, she is able to get Howard's doctor's number from the card and call him.

By appointment, Jimmy and his mother call on Dr. Evans at his office, where Dr. Evans, in a friendly way, performs a physical examination, gives advice on healthful living and finishes up with an immunization to keep Jimmy from getting certain diseases. However, there is no indication of previous tests for an allergic state having been given to the boy before he was immunized. In his experience with the doctor, Jimmy encounters schoolmates who are visiting the doctor for other reasons, and he realizes how helpful his friend the doctor can be.

This motion picture is recommended for the primary grades as a means of helping children understand their relationships to their friend the doctor. It is also recommended for use with adult groups, for it indicates to both child and parent the advantages of cooperating in a school health program of the type presented. It could also be used for the purpose of indicating ideal physician-family and parent-child relations and before medical groups to give them an idea of a suitable attitude toward the school age child. The photography and sound are very well done.

**Breast Plastic: One Stage Operation for Pendulous Breasts:** 16 mm., color, silent, showing time 30 minutes. Produced in 1950 by and procurable from Philip Thorek, M.D., 25 East Washington Street, Chicago 2.

This film illustrates two elementary concepts in the cosmetic reconstruction of hypertrophic pendulous breasts. Most of the film is devoted to an exposure of the detailed surgery for massive hypertrophic pendulous breasts, and it illustrates the technic utilizing the principle of free transplantation of the nipple and areola to its new site. This phase of the moving picture shows a "before" picture of the patient, apparently made from a still photograph.

The operation, as illustrated in this movie, is performed with a simple submammary semilunar incision and amounts to practically an amputation of the breast, leaving just enough breast tissue to be comfortably hammocked by the remaining skin. The free nipple transplant is transferred to the remaining pedicle of the breast. Excellent closeup pictures of the areola and nipples clearly demonstrate a complete take of the nipples. In the cases illustrated, a superficial necrosis with scab formation occurs over each of the transplanted nipples, but these fall off, revealing a take of the areola and nipples.

Several scenes illustrate the patient's condition postoperatively at widely spaced intervals. The remainder of the film demonstrates several other cases in which the nipples were permitted to be attached to the lactogenic portions of the gland. The remaining operations illustrated were apparently all performed as transpositions in which lactogenic function was not interfered with. These latter operations were of the "button hole" type and also involved semilunar incisions at the submammary fold.

A history is presented, illustrating the physical psychological distress of the patient. A title should be included to state that this motion picture illustrates only two plastic surgical operations and that there are many other types which might be suitable. There is some misspelling in the legends, and the illustrations and text are not too convincing in consideration of the rather square breasts that are shown as the result of the operation.

This film may be of interest to general practitioners and general surgeons who are unfamiliar with this type of surgery. It is not recommended for plastic surgeons or medical students. The photography is very good.

**Control of Filariasis in Tahiti:** 16 mm., color, sound, showing time 15 minutes. Prepared by Dr. John F. Kessel. Produced in 1950 by and procurable from Department of Medical Microbiology, School of Medicine, University of Southern California, Los Angeles 7.

This film is entertaining, instructive and presented in good taste. The picture was taken in Tahiti and shows a beautiful tropical setting for the disease. The theme is the teaching of natives to clear the island of mosquitoes and filariasis. Most of the instruction is given by natives to natives using simple line charts labeled in the language of the island. Native singing and scenes blend into the background. Clinical pictures of elephantiasis are impressive. Secondary infection is not mentioned but is clearly visible on the grotesque legs. The mosquito cycle and microfilaria are well demonstrated.

It is a good teaching and propaganda film, of interest to medical students and nurses. Since there is no filariasis in the United States, the appeal to hospital staff groups is somewhat limited. Armed forces personnel, as well as medical travelers to the tropics, would find it of value. It would have a strong appeal to medical missionaries. The photography and narration are very good.

# MEDICAL LITERATURE ABSTRACTS

## AMERICAN

### A.M.A. Am. Journal of Diseases of Children, Chicago

80:719-792 (Nov.) 1950

*Use of Phenurone® in Convulsive Disorders in Children. H. M. Keith. —p. 719.
Tuberculosis in Children. E. Krieger and J. Lapan.—p. 725.
Infantile and Atopic Eczema from Injury to Skin by Overcare and Overtreatment. L. E. Gaul and G. B. Underwood.—p. 739.
Respiration of Full Term and of Premature Infants. H. J. Boutourline-Young and C. A. Smith.—p. 753.
Mediterranean Anemia in Children of Non-Mediterranean Ancestry. H. K. Silver.—p. 767.
*Erythroblastosis Fetalis. VI. Prevention of Kernicterus. F. H. Allen Jr., L. K. Diamond and V. C. Vaughan III.—p. 779.

**Phenacetylurea in Convulsive Disorders.**—Keith reports results of treatment with phenacetylurea (phenurone®) on 35 patients (34 children and one adult) with convulsive disorders. Treatment with other drugs prior to the use of phenacetylurea had not controlled attacks in these patients. The patients were observed for periods varying from three to 20 months. Eight patients (23 per cent) were entirely free from attacks for periods of three to 17 months; 15 (43 per cent) were improved, and 12 were not benefited by the phenacetylurea therapy.

**Prevention of Kernicterus.**—Allen and his associates report that the incidence of kernicterus in erythroblastosis fetalis has decreased as a result of the use of exchange transfusion. The data presented were derived from the study of 368 living Rh-positive babies of sensitized Rh-negative mothers. Severe jaundice occurred in consistent relation to each of the major correlates of kernicterus (high maternal antibody titer, immaturity and male sex). A decrease in the severity of jaundice was observed in babies treated by exchange transfusion. The authors state that this is the probable mechanism for the prevention of kernicterus by exchange transfusion. Their program for the management of erythroblastosis fetalis includes avoidance of early induction of labor, use of exchange transfusion with Rh-negative blood from the female donors for babies likely to have severe jaundice and use of a second exchange transfusion when increasing jaundice is seen following an initial transfusion. Following such a program, the authors observed only one case of kernicterus in a group of 109 babies with erythroblastosis fetalis.

### A.M.A. Arch. Indust. Hyg. & Occupat. Med., Chicago

2:487-620 (Nov.) 1950

Pulmonary Carcinoma in Chromate Workers: I. Review of Literature and Report of Cases. A. M. Baetjer.—p. 487.
Id.: II. Incidence on Basis of Hospital Records. A. M. Baetjer.—p. 505.
Contribution of Charles Turner Thackrah: English Pioneer in Field of Industrial Health. J. W. Brown.—p. 517.
Carbon Disulfide and Hydrogen Sulfide: II. Follow-Up Clinical Study of Low Grade Exposures. H. H. Rubin, A. J. Arieff and F. W. Tauber.—p. 529.
Ears of Industry. R. Carhart.—p. 534.
Handicapped Workers. H. G. Murray.—p. 542.
Experimental Ethylene Oxide Human Skin Injuries. R. J. Sexton and E. V. Henson.—p. 549.
Patch Test—Its Technic and Interpretation. W. Weinberger.—p. 565.
Comparative Toxicity of Five Glycerol Ethers. C. H. Hine, P. Loeb and H. H. Anderson.—p. 574.
Toxicological Studies of Compounds Investigated for Use as Inhibitors of Biological Processes: I. Toxicity of Vinyl Propionate. A. M. Ambrose.—p. 582.
Id.: II. Toxicity of Ethylene Chlorohydrin. A. M. Ambrose.—p. 591.

The Association library lends periodicals to members of the Association and to individual subscribers in Continental United States and Canada for a period of five days. Three journals may be borrowed at a time. Periodicals are available from 1940 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted.

### A.M.A. Archives of Internal Medicine, Chicago

86:649-796 (Nov.) 1950

Effects of Terramycin on Bacterial Flora of Bowel in Man. J. M. Di Caprio and L. A. Rantz.—p. 649.
*Clinical, Functional and Needle Biopsy Study of Liver in Alcoholism. M. Seife, B. J. Kessler and J. R. Lisa.—p. 658.
Use of Choline Supplements in Fatty Metamorphosis of Liver: Needle Biopsy Investigation in Human Beings. B. J. Kessler, M. Seife and J. R. Lisa.—p. 671.
Riehl's Melanosis and Adrenal Glands. L. Spira.—p. 682.
*Hematology of Atomic Bomb Casualties. G. V. LeRoy.—p. 691.
Hemolytic Anemia Secondary to Familial (Hereditary) Defect in Hemoglobin Synthesis: Report of Case with Radioiron Studies. H. Mills, R. L. Huff, M. A. Krupp and J. F. Garcia.—p. 711.
Insulin Resistance: Review of Literature and Report of Case Associated with Carcinoma of Pancreas. J. K. Davidson and E. E. Eddleman. —p. 727.
Liver and Biliary Tract: Survey of Tests for Hepatic Function; Use of Hepatic Star in Differential Diagnosis of Jaundice. C. H. Greene. —p. 743.

**Study of the Liver in Alcoholism.**—The needle biopsy technic for obtaining specimens of the liver was used by Seife and his associates in 63 patients who entered the hospital because of acute alcoholism. Of the 63 patients, 61 were chronic alcoholics. Most of them showed no signs indicative of hepatic disease. All but three of the biopsies were performed within 24 hours of admission. The patients received no therapy other than paraldehyde sedation when necessary and penicillin when indicated. The liver was palpable in seven instances. The results of liver function tests in 20 cases were within normal limits; in the remaining 45, the results of one or more tests were abnormal. Of the 65 initial biopsy specimens, pathological changes were present in 56. The commonest abnormality was fatty metamorphosis, found in 47 cases. The condition was slight in 10, moderate in seven, pronounced in 23 and extreme in seven. Fibrosis was present in 13 cases, was usually focal in distribution and was considered an early cirrhotic lesion. The decrease in fat content was the most prominent feature in results of subsequent biopsies. In 42 patients in whom biopsy revealed fatty metamorphosis initially, 32 showed some degree of fat reduction after one week. Of the 14 patients who underwent a third biopsy seven days after the second, only five showed further but less pronounced decreases in fatty metamorphosis. The decrease occurred despite the absence of specific therapy. Cirrhosis was seen in 21 patients. The focal nature of this lesion, as well as the small amount of tissue provided by needle biopsy, probably explains the fact that cirrhosis was not observed consistently in biopsy specimens from individual patients. Most patients with cirrhosis fell into the classification of steady drinkers. In patients with early cirrhosis, the sulfobromophthalein sodium retention and the albumin to globulin partitions were frequently abnormal. In patients with lesions other than cirrhosis, no correlation between morphological changes and liver function was found.

**Hematology of Atomic Bomb Casualties.**—According to LeRoy, a large number of hematologic studies were performed on Japanese injured by the atomic bombs exploded over Hiroshima and Nagasaki. These studies were conducted by Japanese physicians and by medical officers of the United States Army and Navy. This is the first publication of the complete results. It is possible to describe the syndrome of radiation injury in man in terms of typical clinical symptoms and a typical blood picture. In general, the severity of the symptoms parallel that of the leukopenia. Likewise, the significant symptoms appeared at about the time the lowest leukocyte count was observed. The changes in the thrombocytes paralleled those in the leukocytes. The onset and severity of a hemorrhagic tendency followed closely the variations in the thrombocyte count. The alteration in the red blood cells was less consistent and less useful in diagnosis or prognosis than was the time trend of the leukopenia. From the standpoint of prognosis, the Japanese physicians stated that patients with less

than 500 leukocytes per cubic millimeter were least likely to recover. The data presented here neither support nor deny this clinical observation. In general, the greater the dose of radiation the more profound the blood damage, and the more rapidly the condition develops the more slowly it is repaired. Knowledge of the serial variation in the leukocyte count of the patient is of great clinical importance. It is doubtful that the other elements of the hemogram are of comparable significance. In the event of an emergency, one would be justified in making only leukocyte counts and determinations of hemoglobin, hematocrit and protein by the copper sulfate method. This would be an economical procedure and would provide the information required for evaluation of individual cases and for control of therapy.

## A.M.A. Archives of Pathology, Chicago

**50:**519-656 (Nov.) 1950

Histochemical Studies of Mouse Liver After Single Feeding of Carbon Tetrachloride. R. E. Stowell and C. S. Lee.—p. 519.
Valvular Thrombotic Vegetation in Newborn ("Fetal Endocarditis"). R. H. McDonald.—p. 538.
Brain Metabolism in Vivo: II. Distribution of Lesions Caused by Azide, Malononitrile, Plasmocid and Dinitrophenol Poisoning in Rats. S. P. Hicks.—p. 545.
Range of Extracellular Hydrogen Ion Concentration Tolerated by Macrophages Grown in Tissue Culture. I. N. Dubin and C. K. Yen.—p. 562.
*Myocardial Lesions in Progressive Muscular Dystrophy. W. G. Nothacker and M. G. Netsky.—p. 578.
Candida and Aspergillus Endocarditis, with Comments on Role of Antibiotics in Dissemination of Fungus Disease. L. E. Zimmerman.—p. 591.
Effect of Chorionic Gonadotropin on Transitory Zone of Mouse Adrenal. H. H. Zinsser, A. D. Zinsser and C. M. Storey.—p. 606.
Rickettsiae and Rickettsial Diseases of Man: Survey. Howard Taylor Ricketts Award Lecture, 1950. S. B. Wolbach.—p. 612.

**Myocardial Lesions in Progressive Muscular Dystrophy.**—Nothacker and Netsky say that cardiac lesions occur in progressive muscular dystrophy and resemble the lesions of the striated muscles. They report on four new cases and on two cases previously reported from the Montefiore Hospital, N. Y., by Goodhart and Globus. These six patients were found among 11 patients with progressive muscular dystrophy. The disease developed before the age of 8 in all but one patient, in whom the onset was in early adult life. This confirms the theory that this is predominantly a disease of young men. There was a family history of the disease in four of the six cases. The fact that there was consanguinity for two generations is noteworthy. Two of the patients had transient irregularity of cardiac rhythm, but the others showed no evidence of heart disease.

## Alabama State Medical Assn. Journal, Montgomery

**20:**105-148 (Oct.) 1950

Responsibilities of Radiologist Toward His Patient and Referring Physician in Diagnostic Procedures Involving Gastrointestinal Tract. P. C. Swenson and R. Wigh.—p. 105.
Meningoencephalitis Due to Virus of Herpes Simplex: Report of Case. S. C. Little and J. M. Akin.—p. 115.
Surgical Management of Pancreatitis. C. C. Blackwell.—p. 118.
Treatment of Typhoid Fever: Report of Case. J. M. Humphries and D. H. Sparks.—p. 129.

## American Journal of Medicine, New York

**9:**571-714 (Nov.) 1950

SYMPOSIUM ON TUBERCULOSIS

Biologic and Immunologic Properties of Tubercle Bacilli. R. J. Dubos.—p. 573.
Native and Acquired Resistance to Tuberculosis. M. B. Lurie.—p. 591.
Pathogenetic Concepts of Tuberculosis. E. M. Medlar.—p. 611.
Course and Prognosis of Tuberculosis in Children. E. M. Lincoln.—p. 623.
Effects of Antimicrobial Agents on Tubercle Bacillus and on Experimental Tuberculosis. W. Steenken Jr. and E. Wolinsky.—p. 633.
Antimicrobial Therapy in Human Tuberculosis. H. C. Hinshaw.—p. 654.
Fundamental Principles of Treatment of Tuberculosis, Including Use of Antibiotics. J. M. Jones, W. H. Stearns and A. Himmelstein.—p. 662.
Changing Pattern of Tuberculosis Control. R. J. Anderson.—p. 671.
Renal Physiology: Tubular Transport Mechanisms. J. V. Taggart.—p. 678.

## American Journal of Psychiatry, New York

**107:**321-400 (Nov.) 1950

What Public Health Needs from Psychiatry. H. R. Leavell.—p. 321.
What Psychiatry Needs from Public Health. M. E. Kirkpatrick.—p. 327.
Psychiatry in Public Health. A. Gregg.—p. 330.
Examination of the Accused in Massachusetts (1921-1949). P. B. Hagopian.—p. 336.
Problems of War Neuroses in Light of Experiences in Other Countries. L. B. Kalinowsky.—p. 340.
Treatment in Absence of Pensioning for Psychoneurotic Veterans. T. E. Dancey.—p. 347.
Observations in Treatment of Patients with Psychosomatic Disorders Using Subshock Insulin in Group Setting. H. Sadler and S. Rubin.—p. 350.
Thyroid Function Measured by Serum Precipitable Iodine Determinations in Schizophrenic Patients. E. B. Brody and E. B. Man.—p. 357.
Experimental Rorschach Diagnostic Aid for Some Forms of Schizophrenia. Z. A. Piotrowski and N. D. C. Lewis.—p. 360.
Central Action of Some Antihistamines: Correction of Forced Circling Movements and of Seizure Brain Waves Produced by Intracarotid Injection of Diisopropyl Fluorophosphate (DFP). R. J. Johns and H. E. Himwich.—p. 367.
*Psychodynamic Study of Topectomy Patients: Preliminary Report. J. P. Cattell.—p. 373.

**Psychodynamic Study of Topectomy Patients.**—Cattell reports psychodynamic studies on five psychotic patients before and after subtotal ablation of the frontal cortex. After operation anxiety is less intense and does not pervade so many realms of activity. Obsessive-compulsive, phobic and depressive symptoms are diminished or absent. Emotional response is simplified, with assertiveness, fear and anger appearing more immediately. This is a normalization to the extent that the patient resorts less to repression, displacement, projection and turning against himself. Patients are also less sensitive. In therapeutic sessions they are able to report previously blocked or suppressed material with relative ease. Nevertheless, therapeutic accessibility is not particularly enhanced, for the affective charge is decreased and there is a tendency to intellectualization. Flow of associations with establishment of meaningful links between present occurrences and past experiences is lacking. The patient's dependence on the therapist is increased and has a more childlike quality. Suggestibility is increased. Dynamically, however, the patient is less malleable and is rather indifferent and inelastic in response to interpretations. Dreams are less frequent, and recollection of them is more difficult. Some patients who derived gain from symptoms before operation appear disappointed by the sudden postoperative relief, resenting those who facilitated it and fearing the possibility of achieving emotional independence. The amount of change in any patient is, in part, dependent on the level of integration and functioning before the illness. If the patient had never reached adult functioning, the problem is one of education, not reeducation.

## American Journal of Public Health, New York

**40:**1363-1478 (Nov.) 1950

Public Health and the Laboratory. G. Edsall.—p. 1368.
Diarrhea, Dysentery, Food Poisoning, and Gastroenteritis: Study of 926 Outbreaks and 49,879 Cases Reported to the United States Public Health Service (1945-1947). M. Feig.—p. 1372.
Report on Results of Examinations for Intestinal Parasites. J. A. Kasper, E. J. Cope, M. Lyon and M. White.—p. 1395.
Food Poisoning: Review of 34 Outbreaks. D. M. Griswold.—p. 1398.
*Field Test for Efficiency of Detergents. C. D. Spangler, R. F. Clapp and G. J. Clark.—p. 1402.
*Malaria Eradication in the United States. J. M. Andrews, G. E. Quinby and A. D. Langmuir.—p. 1405.
Public Health Approach to Control of Alcoholism. R. G. McCarthy.—p. 1412.
Opportunities of Industrial Hygiene Section. E.-E. A. Winslow.—p. 1418.
Dental Health Program for Your Community. H. J. Stroud and C. L. Brumback.—p. 1423.
Statistical Study of Factors Influencing Quality of Patient Care in Hospital. M. O'Malley and C. F. Kossack.—p. 1428.

**Field Test for Efficiency of Detergents.**—Spangler and co-workers describe a simple field test for determination of the relative efficiency of detergents used for commercial dishwashing. The test can be conducted with equipment available in a restaurant. It employs effective and representative food soils (peanut butter for fat, partially coagulated egg white for pro-

tein and thin, cooked oatmeal for carbohydrate). A glass is soiled as uniformly as possible, and the soil is set by the heat of a warm air oven at 105 F. for 10 minutes. The glass is then filled half full with a 0.3 per cent by weight solution of the detergent to be tested, made up in water at room temperature. This approximates the concentration recommended for most detergents. The top of the glass is covered with a rubber sink-stopper and shaken vigorously 50 times through a one foot arc. A table shows the results of tests of commercial dishwashing products available on the local market compared with a standard. The test gives comparative rather than exact results but is sufficiently accurate for classification of detergents as good, fair or poor.

**Malaria Eradication in the United States.**—In 1945 the U. S. Public Health Service and the southeastern states initiated a new type of malaria control program. This program in contrast to previous malaria control activities, was aimed not at reduction of the total number of anopheles mosquitos present in the region but rather at killing of those few that actually bite man. In this way they could be prevented from biting human beings a second time, and thus transmitting malaria. Efforts were concentrated on the use of indoor residual dichlorodiphenyltrichloroethane (DDT) sprays in areas where endemic malaria was known to be present or had recently been reported. By 1947, a comprehensive project was under way throughout the Southeast with the objective of eradicating malaria as an endemic disease within five years. A review of the progress, including statistics on malaria mortality and morbidity, diagnostic and survey blood examinations and case appraisals, indicates that endemic malaria has been reduced to the vanishing point. But these data are not sufficiently extensive to prove that malaria has been eradicated from this country.

## Am. Practitioner & Digest of Treatment, Philadelphia

1:1121-1232 (Nov.) 1950

Indications for Treatment in Diseases of Thyroid. J. H. Means. —p. 1121.
Rheumatoid Spondylitis (Strümpell-Marie Arthritis): Orthopedic Management. T. A. Potter.—p. 1129.
Roentgen Treatment and Roentgen Diagnosis of Painful Shoulder. P. S. Friedman.—p. 1133.
Painful Myostatic Dystonia: Diagnostic Problem Treated by Psychotherapy and Unilateral Lobotomy. D. Stafford-Clark.—p. 1137.
The Doctor-Patient Relationship: Its Role in Therapy. A. D. Weisman. —p. 1144.
Hypnosis: Its Evolution and Use in Medicine Today. M. Ross.—p. 1152.
Treatment of Peripheral Arteriosclerosis Obliterans: Physical Agents. A. Fields.—p. 1156.
Treatment of Bronchial Asthma. W. Franklin and F. C. Lowell. —p. 1161.
Multiple Primary Cancer. D. C. Geist, P. J. Grotzinger and F. A. Bothe.—p. 1169.
Effect of Digitalis and Mercurial Diuretic on Electrolyte Balance in Patients with Congestive Heart Failure. D. W. Chapman and C. F. Shaffer.—p. 1172.
Congenital Heart Disease: Clinical and Physiologic Study. H. A. Zimmerman and J. W. Davis.—p. 1178.
Fatal Herxheimer Reaction in Case of Neurosyphilis. S. K. Bush. —p. 1183.
Acquired Hemolytic Anemia with Hypersplenism: Response to Splenectomy. E. S. McCabe and W. H. Erb.—p. 1186.
Etiology and Diagnosis of Headache: Review of Literature. W. A. Huttner.—p. 1190.
Full-Term Abdominal Pregnancy with Delivery of Living Child. E. L. C. Broomes.—p. 1194.

## Angiology, Baltimore

1:373-450 (Oct.) 1950

Diagnosis and Pathogenesis of Obliterative Vascular Disease of Lower Extremities. A. M. Boyd.—p. 373.
Electronic Oscillometer. E. Kasner and J. B. Hersh.—p. 391.
Aneurysm of Abdominal Aorta: Report of Two Cases Treated by "Cutis Grafting." E. L. Lowenberg.—p. 396.
Hemangiomas: Classification, Diagnosis and Treatment. G. T. Pack and T. R. Miller.—p. 405.
Effect of Barbiturates and Other Drugs on Mortality from Diodrast in Mouse. H. H. Ziperman, R. R. Hughes and H. B. Shumacker Jr. —p. 427.
Causes of Failure of Suprarenalectomy and Ganglionectomy in Thrombo-Angiitis Obliterans on Basis of 898 Operations. R. Leriche.—p. 432.
Clinical Grades of Intermittent Claudication. A. H. Ratcliffe.—p. 438.

## Annals of Allergy, Minneapolis

8:583-699 (Sept.-Oct.) 1950

Some Newer Aspects of Biology of Infectious Mononucleosis. L. Pelner and S. Waldman.—p. 583.
Therapy of Ragweed Hay Fever with Electrophoretically Isolated Fractions (Artefolin and Trifidin): Preliminary Report. H. A. Abramson, M. Loebl, H. H. Gettner and B. Sklarofsky.—p. 594.
*Anthocyaninuria and Beet Allergy. G. A. Zindler and G. C. Colovos. —p. 603.
Bronchial Asthma in Small Community Hospitals: Five-Year Survey. W. H. Lipman.—p. 618.
Further Studies on Use of Tissue Culture of Blood Leukocytes in Clinical Evaluation of Bacterial Hypersensitivity of Tuberculin Type. H. Blatt and F. A. Nantz.—p. 622.
*Pyromen in Treatment of Perennial Allergic Symptoms. T. G. Randolph and J. P. Rollins.—p. 626.
Meteorologic Factors in Distribution of Pollens and Molds: Review and Geographic Influence. H. A. Heise and E. R. Heise.—p. 641.
Shortening Treatment of Hay Fever: Combined Antigen-Antihistaminic Technique in Pollen Therapy: Study III. A. L. Maietta.—p. 645.
Fatigue. M. G. Meyer.—p. 649.
Streptomycin Blood Levels in Rabbits Following Administration with an Antihistamine. F. J. Murray, B. Taylor and M. J. Foter.—p. 652.
Nutritional Therapy in Management of Respiratory Anaphylaxis or Allergies. H. N. Vermilye and M. R. Thompson.—p. 654.
Application of Psychodynamic Concepts in Allergy Practice. B. Kraft. —p. 664.
Unusual Allergic Reaction to Penicillin: Case Report. H. Leibowitz and E. Schwartz.—p. 668.
Cosmetic Sensitizers. F. M. Whitacre and R. C. Parsil.—p. 670.
Instrument Devised to Produce Painless Scratches. I. R. Morrison. —p. 679.
Evaluation of Perazil in Allergic Rhinitis. N. J. Ehrlich and M. A. Kaplan.—p. 682.
Prevention of Infectious Asthma. A. E. Fishman.—p. 684.
Allergy to Castor Bean Dust with Report of Case. M. Kaufman.—p. 690.
Molds as Inhalant Allergens. C. H. Kalb.—p. 695.

**Anthocyaninuria and Beet Allergy.**—Zindler and Colovos report a case of anthocyaninuria in a young man with a personal and family history of allergy. For 10 years he had had hay fever in May and June and had recently had hives. Intradermal skin tests with foods and inhalants revealed major sensitivities to wheat, chocolate, string beans and grass pollens. The patient was hospitalized and placed on a diet including wheat and string beans. On one occasion after a meal containing wheat and beets he experienced abdominal cramps, nausea and vomiting. Shortly afterward he had a red bowel movement, and he noted that his urine was the color of port wine. This urine was examined and found negative for blood pigment; it became yellow on alkalinization and red when acidified, in a manner observed with beet juice. After occurrence of these symptoms, wheat, chocolate, string beans and tea were removed from the diet for several days, and beets were given twice daily in an effort to reproduce the condition, but the urine remained normal in color and the patient experienced complete relief from his symptoms. He was then fed string beans along with beets at the same meal. Abdominal cramps, nausea and vomiting promptly followed, and again his urine was port wine colored. The authors found 28 similar cases. Twenty-six were related to beet allergy and two to the ingestion of beets along with foods known to have produced allergic reactions. Clinical reactions were obtained in three patients when beets were fed experimentally, but no anthocyaninuria was detected. Anthocyaninuria seems to depend on the absorption into the blood stream of the pigment from the intestinal tract during the allergic reaction; it is then excreted by the kidney. Normal persons do not absorb detectable quantities of betanin from the intestinal tract. Anthocyaninuria is a valuable sign in the diagnosis of beet allergy. Caution is warranted lest beet sensitivity be produced in the highly food-sensitive patient by the too frequent and copious feeding of beets and beet sugar. Five cases of beet sugar sensitivity are reported.

**Pyromen in Treatment of Allergic Symptoms.**—Interest in the possible therapeutic value of pyromen (a preparation representing the pyrogenic factor obtained from a Pseudomonas species of bacteria) arose from the observation that patients with chills and fever following administration of intravenous fluids appeared to be therapeutically benefited by these reactions. Since pyrogen contamination is the most common cause of chills and fever following venoclysis and since fever has long been recognized as having therapeutic value, an effort was

made to isolate the material responsible for these reactions. This led to the eventual preparation and standardization of pyromen. Initial observations in allergy patients were made employing pyromen in relatively large intravenously administered doses in an effort to obtain febrile responses between 101 and 104 F. Although the therapeutic value of this preparation was impressive, the severity of the chills, muscle ache and fever and the fact that allergic symptoms were sometimes temporarily accentuated following the rather large doses limited its usefulness in the treatment of asthma, dermatitis and other allergic syndromes. Later it became apparent that a more satisfactory clinical response could be obtained with smaller doses, producing few or no constitutional symptoms. The authors discuss their observations on 150 patients who were treated with pyromen for various allergic syndromes. Treatment was continued for 10 days to eight months. The beneficial effect of pyromen on perennial allergic manifestations is evidently the result of stimulation of the pituitary-adrenal system. It is less effective than pituitary adrenocorticotropic hormone or cortisone but is particularly helpful when combined with specific allergy therapy and unlike the pituitary hormone and cortisone is effective when administered orally. Recommended single doses of this pyrogenic material vary from 0.5 to 10.0 gamma (micrograms). Within this range of dosage the febrile response is usually lacking.

## Annals of Surgery, Philadelphia

**132:**849-1008 (Nov.) 1950

Hypothermia: Its Possible Role in Cardiac Surgery: Investigation of Factors Governing Survival in Dogs at Low Body Temperatures. W. G. Bigelow, W. K. Lindsay and W. F. Greenwood.—p. 849.
*The Case for Branchiogenic Cancer (Malignant Branchioma). H. Martin, H. M. Morfit and H. Ehrlich.—p. 867.
Differential Diagnosis of Malignant Bone Tumors. M. B. Coventry.—p. 888.
Acute Volvulus of Small Intestine. Analysis of 36 Cases. W. H. Moretz and J. J. Morton.—p. 899.
Duodenal Fistula. R. B. Brown, R. C. Speir and J. W. Trenton.—p. 913.
Electrophrenic Respiration. V. Effect on Circulation of Electrophrenic Respiration and Positive Pressure Breathing During Respiratory Paralysis of High Spinal Anesthesia. S. J. Sarnoff, J. V. Maloney and J. L. Whittenberger.—p. 921.
Cardiac Resuscitation During Operations for Pulmonic Stenosis. D. A. Cooley.—p. 930.
Technic of Portacaval Anastomosis. W. L. Riker, A. Nielsen and W. J. Potts.—p. 937.
Translumbar Aortic Puncture and Retrograde Catheterization of the Aorta in Aortography and Renal Arteriography. W. E. Goodwin, P. L. Scardino and W. W. Scott.—p. 944.
*Retrograde Aortography with Special Catheter, Including Demonstration of Coronary Arteries. F. Pearl, N. Gray and B. Friedman.—p. 959.
Myotome and Scleratome Pain. J. L. Southworth and S. Krohn.—p. 965.
Surgical Aspects of Calcified Hilar Lymph Nodes. M. G. Buckles.—p. 972.
Surgical Significance of Acanthosis Nigricans. M. Berke and F. B. Wilkins.—p. 980.
Ovarian Vein Phlebothrombosis and Fatal Pulmonary Embolism. W. A. Bailey.—p. 986.
Surgical Therapy of Decubitus Ulcers in Paraplegic Patient. E. S. Marks and C. L. Cogbill.—p. 994.

**The Case for Branchiogenic Cancer.**—According to Martin and co-workers, the term branchiogenic cancer refers to those malignant tumors that are believed to arise in remnants of branchial pouches. Most of the growths considered under this heading are epithelial in character, and therefore the designation branchiogenic carcinoma has been frequently used. The term malignant branchioma is suggested as being more specific, since connective tissue growths could theoretically also arise in branchial remnants. Only 15 (0.3 per cent) of 5,000 cases of primary malignant tumors observed on the head and neck service of the Memorial Hospital, New York, could be regarded as fulfilling the criteria for malignant branchioma: (1) microscopically proved carcinomatous tumor occurring on the lateral aspect of the neck, without any other demonstrable primary lesion, and (2) no recurrence for a period of at least five years after treatment of the cervical tumor alone. Twelve of the 15 patients, 13 men and two women, were over 50. The youngest patient was aged 10 and the oldest 72. It is significant that in all 15 patients the tumor appeared at about the level of the hyoid bone. This is the site of the highest nodes in the internal jugular chain and the site in which cervical metastases are most likely to appear from a primary lesion in the oral cavity or pharynx. There were no anatomic or clinical characteristics differing from those observed in metastatic cervical cancer. None of the patients complained of pain. Irradiation therapy was the method of treatment in 14 of the 15 patients who survived five years or more; only one patient, a girl aged 12 with adenocarcinoma, was subjected to surgery. This suggests that in many, if not all, of the patients receiving irradiation, there was a primary lesion in the pharynx that was controlled by irradiation without ever being discovered. The irradiation dosage was within the cancer lethal range in all cases. The existence of a clinical entity deserving the specific term branchiogenic cancer is entirely hypothetical. A definite diagnosis of branchiogenic cancer cannot be made on a histological basis. The diagnosis of branchiogenic cancer should always remain tentative and should never be considered unless the patient has survived for a period of at least five years after treatment without the discovery of any other primary lesion. A systematic plan for the management of these selected cases of cervical carcinomatous tumors is presented.

**Retrograde Aortography with Special Catheter.**—Pearl and associates used a special catheter for the roentgenographic demonstration of the thoracic aorta, especially its proximal portion, in dogs and in one human subject. This special catheter can be inserted into a peripheral artery and can be guided under fluoroscopic control to any portion of the aorta and many of its larger branches. The catheter has an outside diameter small enough to permit restoration of the artery by suture (2.50 mm.) and a lumen large enough (0.59 mm.) to transmit 5 cc. of fluid per second by manual pressure. It allows one to take selective arteriograms of any portion of the aorta by using only a few cubic centimeters of radiopaque liquid. The coronary arteries may be regularly demonstrated by this method. The arteriograms thus obtained showed excellent contrast, since the vessels visualized were not obscured by an excess of radiopaque medium. The number and severity of reactions from the use of such small amounts of iodopyracet injection (diodrast®) will probably be noticeably reduced. In the authors' case the catheter was inserted through the left radial artery just below the branchial bifurcation and passed to the ascending aorta. Good arteriograms were obtained of the ascending aorta, aortic arch and the left subclavian artery. The intra-arterial catheter offers a safe and efficient method for the selective roentgenographic visualization of the proximal thoracic aorta, arch and descending thoracic aorta.

## Bulletin of Johns Hopkins Hospital, Baltimore

**87:**349-510 (Nov.) 1950

Introduction to Series of Papers on Studies on ACTH and Cortisone. A. M. Harvey.—p. 349.
Effect of Adrenocorticotropic Hormone (ACTH) and Cortisone on Drug Hypersensitivity Reactions. R. A. Carey, A. M. Harvey, J. E. Howard and P. F. Wagley.—p. 354.
Effect of Adrenocorticotropic Hormone (ACTH) and Cortisone on Course of Chronic Bronchial Asthma. R. A. Carey, A. M. Harvey, J. E. Howard and W. L. Winkenwerder.—p. 387.
*Observations on Changes Taking Place in Upper Respiratory Tract of Patients Under ACTH and Cortisone Therapy. J. E. Bordley.—p. 415.
Effect of Adrenocorticotropic Hormone (ACTH) and Cortisone on Course of Disseminated Lupus Erythematosus and Periarteritis Nodosa. R. A. Carey, A. M. Harvey and J. E. Howard.—p. 425.
Effect of Adrenocorticotropic Hormone (ACTH) and Cortisone on Certain Diseases of Eye in Which Hypersensitivity Plays a Role. A. M. Harvey, J. E. Howard and A. A. Kattus.—p. 461.
Action of ACTH and Cortisone on Experimental Ocular Inflammation. A. C. Woods and R. M. Wood.—p. 482
*Cortisone in Experimental Syphilis (Preliminary Note). T. B. Turner and D. H. Hollander.—p. 505.

**Changes in Upper Respiratory Tract During ACTH and Cortisone Therapy.**—Tissue changes in the upper respiratory tract during pituitary adrenocorticotropic hormone therapy were studied in 47 patients with allergic diseases. Approximately 400 examinations were done on this group. Nasal polyps were removed from five patients for examination; nasopharyngeal lymphoid tissue was removed from 16 patients. A total of 47 biopsies were performed at varying intervals during treatment. Routine study included palpation of cervical lymph nodes, inspection of mouth, tongue and throat and transillumination

and roentgenoscopy of the sinuses. The author found that during pituitary adrenocorticotropic hormone therapy the nasal mucous membranes shrink, develop a slate pink color and are covered with a thin layer of clear mucus. Polyps become opaque and pink and begin to shrink, disappearing completely in many cases. Such changes seem to be correlated with the initial eosinopenia developing with pituitary adrenocorticotropic hormone therapy. The nasopharyngeal lymphoid tissue becomes clearly distinct from its surrounding structures, developing an orange-pink color. Discharge around it clears up, and the crypts become more prominent. Within a few days after discontinuation of treatment, the nasal mucosa loses its dusky appearance, and the lymphoid tissue returns to its former state. Nasal polyps return in from two weeks to two months. Cortisone has much the same effect on the tissues of the respiratory tract as does ACTH. Nasal sprays of cortisone result in a slow but definite regression of nasal polyps.

**Cortisone in Experimental Syphilis.**—With cortisone therapy, syphilomas induced in rabbits by intradermal or intratesticular inoculation of Treponema pallidum show striking alterations from the picture usually observed in experimental syphilis. The lesions become soft and spongy; there is an excessive accumulation of a mucoid material tentatively identified as hyaluronic acid; spirochetes are unusually abundant, and the production of Wassermann reagin seems to be inhibited. On withdrawal of cortisone there is a rebound phenomenon in which the lesions reach an unusual size. The evolution of experimental syphilis in the rabbit is a product of the complex interaction of spirochete and host. Under the influence of cortisone this interaction is sufficiently altered for a "dissociation" of parasite and host to occur. The ordinary response of the host to large numbers of spirochetes is partially suppressed, while at the same time spirochetes are multiplying without restraint. This effect may be analogous to those reported by others in pneumococcic pneumonia and in the hypersensitive state. Until more is known about the effect of cortisone on the host-parasite relation in syphilis, it would seem unwise to give the drug to patients with this disease. A "rebound" phenomenon in man could be particularly dangerous, as, for example, in syphilitic involvement of the coronary arteries.

## Bulletin New York Academy of Medicine, New York

**26:**639-700 (Oct.) 1950

Clinical Use of Radioactive Isotopes: Ludwig Kast Lecture. J. H. Lawrence.—p. 639.
Essential Familial Hypercholesterolemia: Cutaneous, Metabolic and Hereditary Aspects. C. F. Wilkinson Jr.—p. 670.
*Antihistamines in Allergic and Non-Allergic Dermatoses. J. Davis.—p. 686.

**26:**703-758 (Nov.) 1950

Early Diagnosis of Cancer in Women: L. Duncan Bulkley Lecture. E. S. L'Esperance.—p. 703.
Common Medical Indications for Therapeutic Abortion. W. E. Studdiford.—p. 721.
Integrative Psychiatry. I. Galdston.—p. 736.

**Antihistamines in Dermatoses.**—According to Davis, it is generally assumed that the mechanism involved in allergic phenomena is the reaction between antigen and antibody in the cellular tissue. As a result of this reaction, a histaminic substance is released. The physiological activities of this agent account for the clinical symptoms of various dermatological allergies. The ability of the antihistamines to counteract these effects led to their use by the dermatologist. The author observed at the New York Hospital and in private practice the effect of both oral and local antihistamine administration on a wide variety of allergic, as well as nonallergic dermatoses. Eight available antihistamine drugs were orally administered and seven were employed in topical applications as well. In all, 666 patients were treated by either oral or local medication or by both. Antihistaminic therapy does not supplant other forms of therapy or the usual routine dermatological care of patients. Therapy with this group of drugs was successful in a large enough percentage of cases and demonstrated enough dramatic relief of symptoms in others to warrant their use. As an additional drug in the therapeutic attack on allergic dermatoses and pruritic symptoms of some nonallergic dermatoses, they are superior to older remedies. The antihistamines should not be used as a substitute for correct diagnosis or thorough investigation. They are contraindicated for local use in generalized or acute dermatoses. Their prolonged use without observation is to be condemned. The antihistamines are not curative, nor do they offer an easy road to determination of a cause.

## Connecticut State Medical Journal, Hartford

**14:**981-1048 (Nov.) 1950

The Doctor and the Social Revolution. P. R. Hawley.—p. 981.
Clinical Diagnosis and Treatment of Disorders of Heart Beat. H. L. Dwyer Jr.—p. 985.
Treatment of Urinary Tract Infections. W. A. Schloss.—p. 994.
"Screening" in the Doctor's Office. B. V. White.—p. 1000.
"Let the State Do It." R. N. Barnett.—p. 1001.
Prostatism Then and Now in New Haven Hospital—1878-1948. H. D. Axilrod and C. L. Deming.—p. 1003.
Child Health Needs. O. L. Stringfield.—p. 1008.

## Gastroenterology, Baltimore

**16:**285-494 (Oct.) 1950. **Partial Index**

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Localization of Referred Pancreatic Pain Induced by Electric Stimulation. W. R. Bliss, B. Burch, M. M. Martin and R. M. Zollinger.—p. 317.

SYMPOSIUM ON GASTROSCOPY

Biopsy Through Flexible Operating Gastroscope. P. L. Shallenberger, C. H. DeWan, C. B. Weed and J. C. Reganis.—p. 327.
Error in Gastroscopic Diagnosis: Consideration of Sources. E. D. Palmer.—p. 341.
*Atropic Gastritis: Follow-Up Study of 100 Patients. J. W. Findley Jr., J. B. Kirsner and W. L. Palmer.—p. 347.
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Comparative Buffering Capacity of Intact and Predigested Protein Following Hourly Feedings. J. S. Levy.—p. 370.
Biliary Cirrhosis. Evaluation of Various "Liver Tests." W. E. Ricketts, J. B. Kirsner and W. L. Palmer.—p. 404.
Site of Formation of Urobilinogen in Intact Human Gastro-Intestinal Tract. O. R. Hollan.—p. 418.
Problems in Diseases of Small Bowel. Clinical Picture of Unusual Cases of Diseases of Small Bowel. M. A. Spellberg and E. L. Jackson.—p. 425.
Factors Influencing Mortality Rate of Perforated Peptic Ulcer. R. P. Reynolds, M. O. Cantor and C. Stebbins.—p. 440.
Visualization of Ileocecal Papilla in Living Subject. A. W. Ulin and J. Deutsch.—p. 444.
Spontaneous Rupture of Esophagus. With Report on Two Cases. F. W. Mulsow.—p. 450.
Effect of Human Serum Albumin and Mercurial Diuretics on Ascites in Patients with Hepatic Cirrhosis. W. P. Havens Jr., and L. W. Bluemle.—p. 455.
Cardiospasm. Review of 100 Cases. E. C. Sifers and G. Crile Jr.—p. 466.
Excretion and Concentration of Aureomycin in Abnormal Human Biliary Tract. J. Zaslow, T. H. Hewlett and R. W. Lorry.—p. 475.
Relation to Pancreatic Secretion to Peptic Ulcer Formation. III. Influence of Hyperglycemic-Glygenolytic Factor. E. J. Poth and S. M. Fromm.—p. 490.

**Urecholine® as Stimulant.**—Kyle and his associates describe the use of bethanechol chloride (urecholine,® urethane of β-methylcholine chloride) as a stimulant of the external secretion of the pancreas in 18 control patients in whom there was no clinical or laboratory evidence of pancreatic, hepatic or biliary tract disease. Subcutaneous injection of a 10 mg. dose of the drug was followed by an increase in the volume of juice aspirated from the duodenum, in flow of pancreatic juice and of bile, in the alkaline $p_H$ of the duodenal juice, in the concentration of enzymes per milliliter, in the total output of enzymes per minute, in the volume of gastric content and decrease in free and total acidity. The point at which bethanechol chloride begins to exert a maximal effect varies from five to 15 minutes and is dependent on the rate of absorption from the subcutaneous tissues.

**Atrophic Gastritis.**—One hundred patients with atrophic gastritis without pernicious anemia were followed by Findley and his co-workers from five to 14 years (average 8.5 years). Follow-up gastroscopic and/or roentgenologic examinations

were made of 54 of the patients. No malignant tumors were detected, although benign-appearing gastric polyps were discovered in two persons six and nine years after the initial diagnosis of atrophic gastritis. Pernicious anemia did not develop in any of the patients. Atrophy of the mucosa appeared unchanged in 23, more pronounced in 13 and improved in six. Gastric secretion in response to histamine was measured at intervals of five to 14 years in 28 patients. The acid output declined in 14 of the 17 patients who initially secreted free acid. No parallelism was discovered between the appearance of the gastric mucosa and the patient's symptoms.

## GP (J. Am. Acad. of Gen. Practice), Kansas City, Mo.

**2**:1-146 (Nov.) 1950

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Early Symptoms of Acute Appendicitis. B. O. Hawk and E. L. Keyes. —p. 59.

## Illinois Medical Journal, Chicago

**98**:269-320 (Nov.) 1950

Clinical Significance of Femoral Hernia. M. E. Lichtenstein and K. H. Frankhauser.—p. 278.
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*Methemoglobinemia in Infants. A. R. Eveloff.—p. 294.
Familial Hereditary Hemorrhagic Telangiectasia in the Negro: Report of Case. W. H. Kleinschmidt and S. O. Schwartz.—p. 298.
*Maternal Pulmonary Embolism by Amniotic Fluid. C. Newberger. —p. 301.
Actinomycotic Brain Abscess. M. Tinsley and A. Froman.—p. 303.
Appendiceal Abscess in Four Month Old Infant. M. P. Borovsky. —p. 307.
Dislocation of Lumbo-Sacral Spine. S. L. Goldberg.—p. 311.
Idiopathic Thrombocytopenic Purpura: Associated with Accessory Spleens and Complicated by Severe Hemothorax and Hemoperitoneum. G. C. Coe, J. T. Gault and H. J. Hirshfield.—p. 313.

**Methemoglobinemia in Infants.**—Methemoglobinemia may occur in young infants as a result of the ingestion of well water containing excessive amounts of nitrates. This produces cyanosis, which may be attributed erroneously to congenital heart disease, intracranial hemorrhage, abnormalities of the respiratory tract or even enlarged thymus. Once attention is focused on this as a possible causative factor in cyanosis, the relative frequency of this condition is recognized. Eveloff describes observations on 25 such infants who were admitted to hospitals in Springfield during a period of about two years. All the infants came from rural homes in which a well, in most instances an unsatisfactory one, was the source of the water. All these babies were being given artificial milk formulas, using either evaporated or powdered milk. The first symptom noted in all cases was cyanosis, which as a rule was gradual in onset. There was no close relation between the quantity of nitrate present in the water and the time of onset or degree of symptoms. Nitrate levels varied from 99 parts per 1,000,000 to 1,050 parts per 1,000,000. There were two deaths in the 25 cases. The histories in these two cases strongly suggest that an earlier, correct diagnosis would have prevented these fatalities. Treatment consisted of oxygen therapy and the intravenous administration of methylene blue, in a dosage of 1.0 to 2.0 mg. per kilogram of body weight. Methylene blue was given orally to several patients. The poor quality of the wells in the Sangamon County area, as shown by nitrate content determination of samplings, probably accounts for the relative frequency of methemoglobinemia in infants in this area.

**Maternal Pulmonary Embolism by Amniotic Fluid.**—Newberger describes the twentieth case on record of pulmonary embolism resulting from particulate matter in the amniotic fluid. The patient, aged 40, was a quadrigravida and had two living children. She entered the hospital, not in labor, but because of her worry at being "overdue." Medication for induction of labor was started at 4 p. m. with 5 grains (300 mg.) of quinine every hour for four hours, followed by posterior pituitary (pituitrin®), given every 30 minutes. Irregular contractions began at 12:50 a. m., and by 1:30 a. m. they occurred at five-minute intervals. At 2:15 a. m. the membranes ruptured; there was a large amount of dark, bloody discharge, and the patient was nauseated. At 2:45 a. m. she had sudden twitchings of the arms and became cyanotic. She was given oxygen, a 25 per cent solution of nikethamide (coramine®), epinephrine (adrenalin®) into the heart and artificial respiration, but death occurred at 3:00 a. m. At 3:05 a. m. a postmortem midforceps operation was done, with the extraction of a living, 7 pound 7 ounce (3,374 Gm.) male infant. Microscopic section from blocks of lung tissue showed the lumen of many arterioles and capillaries filled with squamous epithelial cells, mucus, amorphous debris and blood cells, characteristic of the composition of emboli due to amniotic fluid.

## Journal of Gerontology, Springfield, Ill.

**5**:203-265 (July) 1950

Aging of Elastic Tissue in Human Skin. C. K. Ma and E. V. Cowdry. —p. 203.
Significance of Medial Age Changes in Human Pulmonary Artery. A. I. Lansing, T. B. Rosenthal and M. Alex.—p. 211.
Age Changes in Pupil Size. J. E. Birren, R. C. Casperson and J. Botwinick.—p. 216.
Urinary Neutral 17-Ketosteroids in Aged. K. Kowalewski.—p. 222.
Stability of Body Function in Aged: Effect of Exposure of Body to Cold. C. L. Krag and W. B. Kountz.—p. 227.
Vitamin Studies in Middle-Aged and Old Individuals: Clinical Studies in Hypovitaminemia $B_1$. J. E. Kirk and M. Chieffi.—p. 236.
Mortality in Traumatic Abdominal Injuries in the Elderly. D. D. Collins.—p. 241.
Pasteboard Leg Prosthesis for Elderly Patients. O. V. Raagaar.—p. 245.
Personal Adjustment of Recipients of Old Age Assistance. E. Shanas. —p. 249.
Attitudes of Superior Groups Towards Retirement and Old Age. A. R. Chandler.—p. 254.
Medical Organization of Modern Home for Aged. F. D. Zeman. —p. 262.

## Journal of International College of Surgeons, Chicago

**14**:491-634 (Nov.) 1950. **Partial Index**

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Intracanalicular Tumors of Mammary Gland: Clinical Diagnosis and Histopathologic Picture. J. Medina and J. S. Góes Jr.—p. 507.
Outlook for Patients with Leiomyomas of Stomach. L. H. Appleby. —p. 512.
Immediate Ambulation After Celiotomy. C. J. Bellis.—p. 517.
Culdoscopy with Spinal Anesthesia. J. F. Shanaphy and J. F. Ziemba. —p. 527.
Subdiaphragmatic Perforation of Esophagus: Importance of Jejunal Alimentation in Delayed Surgical Treatment. L. River.—p. 533.
Local Asphyxia and Chemotherapy for Clinical Tumors. F. M. Allen. —p. 538.
Leiomyosarcoma of Jejunum. R. M. Fleming and J. R. Pearson.—p. 547.
Use of Oxidized Cellulose to Control Hepatic Bleeding. B. J. Ficarra. —p. 554.
Surgical Management of Concomitant Strabismus. D. T. Atkinson. —p. 557.
Suction Feeding Tube Employed in Gastrointestinal Surgery. L. A. Frankel.—p. 568.
Vagotomy: Experimental Work, Research, Clinical Application and Results. A. M. Hansen.—p. 577.
Study and Treatment of Spasmodic Paraplegia Following Pott's Disease. J. G. Zacharakopoulos.—p. 596.
*Phrenic Nerve Crush as Adjunct to Vagotomy in Treatment of Peptic Ulcer. U. G. Dailey.—p. 600.
Uterotubal Studies Using Lipiodol. J. C. Brougher.—p. 603.
Positional Anomalies of Large Intestine: Their Clinical Significance. W. Sheinfeld.—p. 608.
Rhinoplastic Approach to Cleft Lip Problem. S. Segal Jr.—p. 613.

**Phrenic Nerve Crush and Vagotomy in Peptic Ulcer.**—Studies on dogs revealed that cutting of the phrenic nerve at the time that a vagotomy is performed will prevent the postoperative atony, gastrectasia and stasis that often develop after vagotomy. Dailey therefore decided to combine phrenic crush with vagotomy in operations on five patients with recurrent duodenal ulcer. Gastroenterostomy was also performed. All these patients had an exceptionally smooth convalescence. The temporary paralysis of the left side of the diaphragm caused by crushing of its motor nerve adds materially to the space within

the abdomen required for the expanded stomach and permits the latter to assume a vertical position, favoring drainage. A further beneficial effect of phrenic interruption is the resulting relaxation of the "pinchcock" mechanism at the cardia. The author admits that vagotomy has its limitations and restricts it to the treatment of chronic cicatrizing ulcer resisting medical management.

## Journal of Investigative Dermatology, Baltimore

15:265-342 (Oct.) 1950

Medical Specialty Research in University: Its Organization and Support in Department of Dermatology. D. M. Pillsbury.—p. 275.
Intensive Panthenol Therapy of Lupus Erythematosus. L. Goldman. —p. 291.
Sodium Para-Aminobenzoate Therapy of Atopic Dermatitis. Preliminary Report. A. L. Weiner.—p. 295.
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Relative Effect of Local Anesthetics on Experimental Histamine Pruritus in Man. W. B. Shelley and F. M. Melton.—p. 299.
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Bacterial Flora of Normal Human Skin. C. A. Evans, W. M. Smith, E. A. Johnston and E. R. Gibiett.—p. 305.
Effect of Topical Antipruritic Therapy on Experimental Induced Pruritus in Man. F. M. Melton and W. B. Shelley—p. 325.
Atopic Dermatitis: II. Role of Sweating Mechanism. L. Tuft, H. S. Tuft and V. M. Heck.—p. 333.
Therapeutic Assays of Skin and Cancer Unit of New York University Hospital: Assay IV. Aureomycin Hydrochloride Ointment. H. H. Sawicky, F. Pascher, L. Frank and B. Rosenberg.—p. 339.

## J. Neuropathology & Exper. Neurology, Baltimore

9:353-452 (Oct.) 1950. **Partial Index**

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Meningiomas of Sphenoidal Ridge: Clinicopathologic Study. E. D. Horning and J. W. Kernohan.—p. 373.
Heredopathia Atactica Polyneuritiformis. H. Reese and J. Bareta. —p. 385.
Effect of Streptomycin on Tuberculous Meningitis: Pathologic Study. A. Levinson, J. A. Luhan, W. P. Mavrelis and H. Herzon.—p. 406.
Capillary Resistance Studies in Multiple Sclerosis. M. H. Shulman, L. Alexander, O. F. Ehrentheil and R. Gross.—p. 420.
Cortico-Cortical Connections of Cortex Buried in Intraparietal and Principal Sulci of Monkey (Macaca Mulatta). O. Sugar, R. Petr, L. V. Amador and B. Griponissiotis.—p. 430.
Effect of Intravenous Urea on Cerebrospinal Fluid Pressure in Monkeys. L. Smythe, G. Smythe and P. Settlage.—p. 438.
Meningothelial Meningioma of Fourth Ventricle. F. S. Vogel and L. D. Stevenson.—p. 443.

## Journal of Pediatrics, St. Louis

37:685-818 (Nov.) 1950

Some Practical Aspects of Allergy. S. C. Dees.—p. 685.
Relation of Hyaluronidase to Salicylates and Rheumatic Fever. A. A. Jaworski, J. E. Farley Jr., J. Barrett and R. A. Jaworski.—p. 697.
Postvaccinal Encephalitis in Infancy. H. J. Lawler.—p. 709.
Feeding of Premature Infants: Use of Simple Formula. S. M. Abelson. —p. 711.
Sensitivity to Diphtheria Bacilli and Related Organisms to Nine Antibiotics. G. G. Jackson, Chang Shih-Man, E. D. Place and M. Finland. —p. 718.
Use of Neo-Synephrine in Paroxysmal Supraventricular Tachycardia. G. C. Cunningham and W. F. Schnitzker.—p. 727.
Effect of Adrenocorticotropic Hormone in Epilepsy. R. Klein and S. Livingston.—p. 733.
Testosterone in Progressive Pseudohypertrophic Muscular Dystrophy. M. A. Perlstein and H. Gutterman.—p. 743.
Treatment of "Colic" in Infancy by Use of Pacifier. M. I. Levine and A. I. Bell.—p. 750.
Acute Thallotoxicosis: Report of Two Cases Treated with BAL. J. A. Welty and B. H. Berrey.—p. 756.
Prenasal and Preoral Auscultation. J. L. Wilson.—p. 759.
Ammonia Dermatitis: Treatment with Diaparene Chloride Ointment. M. L. Niedelman and A. Bleier.—p. 762.

**Adrenocorticotropic Hormone in Epilepsy.**—Klein and Livingston decided to test the effects of pituitary adrenocorticotropic hormone (ACTH) in patients with epilepsy because, on the one hand, the administration of pituitary adrenocorticotropic hormone produces a metabolic state superficially similar to that produced by a ketogenic diet, which has proven helpful in epilepsy, and, on the other hand, cortisone and pituitary adrenocorticotropic hormone have been shown to alter the electroencephalogram in conditions other than epilepsy. Since other investigators had obtained favorable results with desoxycorticosterone acetate in epilepsy, it was decided to test this substance as well. Six epileptic children were treated with these hormones. Four were objectively benefited when treated with pituitary adrenocorticotropic hormone. The patient with simple petit mal showed no definite improvement. The other patient, who was not relieved by treatment, received apparently adequate amounts of desoxycorticosterone acetate and cortisone, but could not tolerate pituitary adrenocorticotropic hormone for more than four days because of side effects. This patient was then given a ketogenic diet. She had no more convulsions, and her electroencephalogram became normal. The patients who did respond to pituitary adrenocorticotropic hormone demonstrated many types of brain waves and clinical manifestations of epilepsy. Some had grand mal, with or without petit mal, and/or psychomotor seizures. One had only psychomotor attacks. Another patient had frequent grand mal seizures, which stopped while he was receiving pituitary adrenocorticotropic hormone. This patient had an essentially normal electroencephalogram before and after treatment. When treatment was stopped, his condition became immediately much worse than before therapy. The improvement achieved lasted for varying lengths of time. One patient had a clinical relapse in one day. The improvement in electroencephalogram pattern lasted for periods up to two weeks. No certain clinical benefit could be demonstrated for any significant period after the drug was withdrawn.

## Journal Pharmacology & Exper. Therap., Baltimore

100:119-250 (Oct.) 1950. **Partial Index**

Pharmacological and Toxicological Studies on 2-(N-p'-tolyl-N-(m'-Hydroxyphenyl)-Aminomethyl)-Imidazoline (C-7337), New Adrenergic Blocking Agent. J. H. Trapold, M. R. Warren and R. A. Woodbury.—p. 119.
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Estimation of Activity of Analgetic Materials. D. D. Bonnycastle and C. S. Leonard.—p. 141.
Antiaccelerator Cardiac Action of Quinine and Quinidine. O. Krayer. —p. 146.
Comparison of Anticonvulsant Actions of Some Phenylhydantoins and Their Corresponding Phenylacetylureas. E. A. Swinyard and J. E. P. Toman.—p. 151.
Histochemical Differentiation of Types of Cholinesterases and Their Localizations in Tissues of Cat. G. B. Koelle.—p. 158.
Renal Clearance and Plasma Protein Binding of Aureomycin in Man. J. H. Sirota and A. Saltzman.—p. 210.
Rate of Penetration of Barbituric Acid Derivatives into Brain. T. C. Butler.—p. 219.

## Northwest Medicine, Seattle

49:655-736 (Oct.) 1950

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Interpulmonary Breathing, Sign of Bronchial Obstruction. W. S. Butts. —p. 684.
Food-Borne Typhoid Outbreak with Rapid Dissemination of Cases Through Air Transportation. R. B. Williams, L. A. Morley and M. Kohler.—p. 686.
Treatment of Typhoid Carrier State. C. C. Pearson and W. A. Wolfe. —p. 689.
Typhoid Fever Treated with Chloromycetin, Sulfathalidine and Penicillin. S. M. Lancefield and F. K. Power.—p. 691.

## Plastic and Reconstructive Surgery, Baltimore

6:255-338 (Oct.) 1950. **Partial Index**

Rhytidoplasty. D. M. Mayer and W. A. Swanker.—p. 255.
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Traumatic Avulsion of Skin of Male External Genitalia: Coverage with Local Remnants of Genital Skin. J. M. Bruner.—p. 334.

## Proc. Soc. Exper. Biol. & Med., Utica, N. Y.

75:1-304 (Oct.) 1950. **Partial Index**

Standardization of $I^{131}$ Solutions by Direct Comparison of Gamma Activities. W. A. Reilly, D. I. Bayer and J. M. Siegel.—p. 1.
Plasma Levels of Free Amino Acids in Normal Subjects Compared with Patients with Rheumatoid Arthritis. A. L. Borden, E. B. Wallraff, E. C. Brodie and others.—p. 28.
*Effect of Cyclopropane, Ether, and Thiopental Sodium upon Over-Digitalized Heart. L. Mosey and J. W. Stutzman.—p. 34.
Effect of ACTH on Glycogenesis and Glycolysis in Hypophysectomized Rats. L. G. Abood and J. J. Kocsis.—p. 55.
Influence of Blood Incompatibilities on Measurement of Blood Volume by Cell-Tagging Methods. J. L. Nickerson, M. I. Gregersen, W. S. Root and L. M. Sharpe.—p. 61.
Diurnal Variation in Plasma Iron Level in Man. L. D. Hamilton, C. J. Gubler, G. E. Cartwright and M. M. Wintrobe.—p. 65.
Excretion of Phenylalanine and Derivatives in Phenylpyruvic Oligophrenia. G. A. Jervis.—p. 83.
Comparison of Influenza B Virus Strains from the 1950 Epidemic with Strains from Earlier Epidemics. I. Tamm, E. D. Kilbourne and F. L. Horsfall Jr.—p. 89.
Hypoadrenalism: Steroidal Mediation of Sodium Action on Blood Pressure; Modification of Antiarthritic Response to Cortisone. G. A. Perera and C. Ragan.—p. 99.
Use of Monosodium Glutamate for Improving Palatability of Amino Acid Rations. S. C. Smith and C. A. Elvehjem.—p. 103.
*Production of Specific Antisera Against Sickle Cell Anemia Erythrocytes; Antibody in Sicklemia Sera. R. G. Schneider and W. C. Levin.—p. 110.
*Effect of X Radiation on Antibody Formation. L. O. Jacobson, M. J. Robson and E. K. Marks.—p. 145.
*Inhibitory Effect of Cortisone on Anaphylaxis in Mouse. C. T. Nelson, C. L. Fox Jr. and E. B. Freeman.—p. 181.
Effect of Cortisone and ACTH on Eosinophils and Anaphylactic Shock in Guinea Pigs. M. Dworetzky, C. F. Code and G. M. Higgins.—p. 201.
Antipyretic Effect of Cortisone. L. Recant, W. H. Ott and E. E. Fischel.—p. 264.
Electron-Microscopic Examination of Human Milk Particularly from Women Having Family Record of Breast Cancer. L. Gross, A. E. Gessler and K. S. McCarty.—p. 270.
Development of Fatty Livers in Fasted Male Mice Bearing Transplantable Lymphosarcoma. E. Adams.—p. 282.
Urinary Excretion of Certain Amino Acids During ACTH and Cortisone Treatment of Rheumatoid Arthritis. E. C. Brodie, E. B. Wallraff, A. L. Borden and others.—p. 285.

**Effect of Anesthetics on Digitalis Arrhythmias.**—Mosey and Stutzman digitalized dogs to cardiac toxicty with ouabain (0.07 or 0.08 mg. per kilogram) or with digitoxin (0.3 mg. per Kg.) and then anesthetized them with cyclopropane, ether or thiopental sodium. Cyclopropane improved or abolished the arrhythmias produced by digitalis preparations. Ether caused a reversion to normal rhythm. Thiopental sodium had no effect on the electrocardiographic abnormalities of over-digitalized dogs.

**Immunologic Studies of Sicklemia.**—Schneider and Levin found that erythrocytes from two persons with sickle cell anemia, when injected into rabbits, produced antiserums that agglutinated erythrocytes of 19 patients with sickle cell anemia, but not those of 21 persons with sickle cell trait nor those of 124 normal persons. The authors believe that such serums may be useful in the differentiation of sickle cell anemia and sickle cell trait. The presence of agglutinin antibody was demonstrated in the serums of all of 13 patients with sickle cell anemia. This may explain the hemolysis that is characteristic of this disease. Of 11 patients with sickle cell trait, four had agglutinin antibodies in their serums and two had doubtful agglutinin antibodies.

**Effect of Roentgen Irradiation on Antibody Formation.**—It has been shown that total body exposure to ionizing radiation suppressed the usual antibody response to antigens when these were injected shortly before or shortly after irradiation. This suppression has been attributed to the destructive effect of irradiation on lymphatic tissue and bone marrow. This report contains studies on the capacity of rabbits to form antibodies after the whole body, except for the spleen or appendix, has been exposed to 800 r radiation. It was demonstrated that if the spleen or appendix of the rabbit is protected by lead shielding during total body irradiation, the capacity to produce antibodies to an antigen is retained to a considerable degree even though lymphatic tissue elsewhere in the body is temporarily destroyed.

**Cortisone and Anaphylaxis.**—Nelson, Fox and Freeman observed that administration of cortisone to sensitized mice 18 hours before intravenous injection of a challenging dose of antigen prevented fatal anaphylactic shock in 38 out of 42 animals. In contrast, 28 of 34 sensitized but unprotected control mice died in anaphylactic shock.

## Psychoanalytic Review, Albany, N. Y.

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Some Aspects of Homosexualtiy in Relation to Hypnosis. J. M. Schneck.—p. 351.
What Comes After Dilantin? T. E. Uniker.—p. 363.

## Quart. Bull. of Sea View Hospital, Staten Island, N. Y.

11:129-168 (Oct.) 1950

*Complications and Sequelae of Primary Pulmonary Tuberculosis: Review of 600 Cases. P. I. Tsai and W. J. Bashe Jr.—p. 129.
Pathology of Excised Tuberculous Pulmonary Specimens: Review of 127 Specimens Resected for Pulmonary Tuberculosis. S. H. Stern and T. Ehrenreich.—p. 149.
New Technique for Preservation of Pathologic Specimens in Dry State. B. Sills and G. Gold.—p. 159.

**Complications of Primary Pulmonary Tuberculosis.**—Tsai and Bashe discuss, on the basis of 600 cases, complications and sequelae that occur in children after a primary tuberculous infection. The mortality was 2.5 per cent. Pulmonary cavitation occurred at the site of the primary focus in 4 per cent of the children. It was associated with a high incidence of hematogenous dissemination but more often with bronchogenic spread. The radiological shadow of "epituberculosis" was frequently seen. This condition, frequently ascribed to an allergic, nonspecific perifocal reaction, was often indistinguishable from atelectatic or caseous areas and probably represents varying degrees of each of these three elements. Bronchial distortion with ectasis and stenosis occurred at the site of large primary foci. These were asymptomatic conditions even up to two years after development. Miliary pulmonary tuberculosis (seven cases, 1.2 per cent) occurred as a part of massive hematogenous dissemination. Four patients died, all before the use of streptomycin. Tuberculous meningitis (14 cases, 2.4 per cent) was often seen as a terminal stage of miliary disease. It usually occurred while the primary lesion was relatively fresh but was also found in association with a healing focus. All the patients who were treated before the introduction of streptomycin died; one half the patients (four cases) in whom it was used lived. Bone tuberculosis was present in 49 (8.2 per cent) of the patients. Although considered a late manifestation of the disease, it was found in conjunction with early as well as healed primary lesions. Involvement of the spine occurred most frequently.

## South Dakota Journal of Medicine, Sioux Falls

3:263-284 (Sept.) 1950

Neuritis. L. J. Karnosh.—p. 263.

3:285-320 (Oct.) 1950

Post-Operative Wound Dehiscence and Eventration: Report of 28 Cases. J. A. Kittelson and H. O. Kittelson.—p. 286.
Purpura Hemorrhagica: Current Knowledge Concerning Blood Coagulation and Its Relation to Various Hemorrhagic Diatheses with Emphasis on Idiopathic Thrombocytopenic Purpura. M. E. Sanders.—p. 292.
Diverticula of Small Intestine. C. S. Larson.—p. 296.

## Southwestern Medicine, El Paso, Texas

31:313-348 (Oct.) 1950

Experimental Cancer Research and Its Contribution to Knowledge of Cancer. E. T. Bell.—p. 327.
Rupture of Uterus with Two Unusual Cases. E. G. McCarthy.—p. 330.

31:349-384 (Nov.) 1950

Office Urology. E. Belt.—p. 363.
Cerebral Palsy. W. L. Minear.—p. 367.

31:385-420 (Dec.) 1950

Injuries to Elbow Region. I. W. Kaplan.—p. 400.
Renal Complications from Sulfonamides (Crystalluria and Lower Nephron Nephrosis). R. F. Thompson.—p. 403.

## FOREIGN

### British Heart Journal, London

12:317-440 (Oct.) 1950

Effect of Digoxin on Right Ventricular Pressure in Hypertensive and Ischaemic Heart Failure. R. I. S. Bayliss, M. J. Etheridge, A. L. Hyman and others.—p. 317.
Cor Triatriatum: Concerning Nature of Anomalous Septum in Left Auricle. C. G. Parsons.—p. 327.
Universal Vector Cardiograph. A. G. T. Becking, H. C. Burger and J. B. Van Milaan.—p. 339.
Venous Hums in Hepatic Cirrhosis. H. J. G. Bloom.—p. 343.
Genesis of Electrocardiogram of Right Ventricular Hypertrophy. M. McGregor.—p. 351.
Fatal Case of Delayed Hypersensitive (Anaphylactic) Reaction to Test Dose of Vasiodone. A. C. A. Coombes and E. H. Roche.—p. 360.
Effort Test in Angina Pectoris. P. Wood, M. McGregor, O. Magidson and W. Whittaker.—p. 363.
Angiocardiograms After Ligation of Ductus Arteriosus. K. D. Keele. —p. 372.
*Valvulotomy for Pulmonary Valvular Stenosis. R. C. Brock and M. Campbell.—p. 377.
*Infundibular Resection or Dilatation for Infundibular Stenosis. R. C. Brock and M. Campbell.—p. 403.

**Valvulotomy for Pulmonary Valvular Stenosis.**—Brock and Campbell describe the clinical picture of pulmonary valvular stenosis with closed interventricular septum. Depending on its severity and on whether the foramen ovale is sealed or potentially patent, the disability may be slight or extreme, the patient may be cyanotic or not and the cyanosis may date from childhood or may develop in early adult life. The heart may be slightly or greatly enlarged, and the electrocardiogram may show slight or gross signs of right ventricular preponderance. The differentiation between pure pulmonary stenosis and Fallot's tetralogy with infundibular or valvular stenosis is discussed. In Fallot's tetralogy the stenosis is generally infundibular but is occasionally valvular. The authors describe an operation designed to relieve valvular stenosis. They emphasize that the diaphragm formed by the stenosed valve is merely cut across transversely, leaving two wide cusps that allow the valve to remain patent. No part is excised, as this might cause serious regurgitation. The operation has been done on 33 patients, 18 with pulmonary stenosis alone and 15 with valvular stenosis as part of Fallot's tetralogy. The operative mortality was high in the patients with large hearts and congestive failure. In younger patients in whom the condition had not progressed so far, the risks were much less, and 23 patients survived and were improved. The success of the operation is difficult to judge in the first two or three weeks, but soon thereafter a fair estimate can be obtained. There can be no doubt that pulmonary valvulotomy is good treatment for pulmonary stenosis, either alone or in combination with Fallot's tetralogy. The final decision as to the best procedure will come from a longer follow-up of these and other cases. Some temporary changes in the electrocardiogram, suggesting muscle injury, are seen during the few weeks following operation; these disappear in the standard but not always in the chest leads. In patients over 20 years of age, the risks of operation are much greater and the chance of good results much less than in those under 10 years of age.

**Infundibular Resection or Dilatation for Infundibular Stenosis.**—When pulmonary stenosis occurs as one of the components of Fallot's tetralogy, the obstruction is usually not at the valves but in the infundibular portion of the right ventricle. The Blalock-Taussig operation short-circuits this stenosis by anastomosis of a systemic to a pulmonary artery. A simpler procedure and one that gives better blood flow to the lungs is described by Brock and Campbell. This consists of relief of the infundibular stenosis by direct resection. Generally, the ventricular wall is incised and a small probe passed to confirm the presence and level of the obstruction. A punch is inserted, opened and directed through the stenosis. When the instrument is closed, the resected portion of tissue is held secure and is withdrawn with the instrument. In this way the authors have been able to resect almost the whole circumference of the stenosed area in one section or in several sections. The punch, when closed, can also be passed up to the valve level, so that the presence of a valvular obstruction may be ascertained, or a free passage into the pulmonary artery demonstrated. In several cases the little finger has been inserted to palpate the stenosed area and to dilate it further. In two patients with only mild stenosis dilatation without resection appeared to be adequate; good results have followed. Eleven patients have been subjected to resection or dilatation. Three patients died after operation. All were over 20 years of age. In younger patients the operation does not seem to be as dangerous as might be expected. Seven of the eight survivors, who have been followed for from 11 to 18 months after operation, have benefited greatly.

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

### British Journal of Radiology, London

23:579-626 (Oct.) 1950

Congenital Anomalies of Tarsal Navicular with Particular Reference to Calcaneo-Navicular Coalition: C. H. Chambers.—p. 580.
Fractures of Femoral Neck Following Pelvic Irradiation: Review of 10 Cases. W. D. C. McCrorie.—p. 587.
System of Dosage Estimation for Tangential Irradiation of Breast Without Bolus. K. H. Clarke.—p. 593.
Calcino-Universalis: Type Lipo-Calcino-Granulomatosis. S. F. Oosthuizen, P. le Roux and A. S. de Wet.—p. 598.
Ionization Measurements at Very High Intensities: I. Pulsed Radiation Beams. J. W. Boag.—p. 601.
Study of Normal and Pathological Organs by Means of Radio-Opaque Plastic and Stereoscopic X-Ray Films. B. A. Dormer and K. Weinbren.—p. 612.

### British Medical Journal, London

2:1015-1072 (Nov. 4) 1950

Rare Forms of Paroxysmal Trigeminal Neuralgia and Their Relation to Disseminated Sclerosis. W. Harris.—p. 1015.
*Prolonged Treatment of Rheumatoid Arthritis with ACTH Alone and with Gold. J. Goslings, W. Hijmans, P. M. v. Limpt and H. A. v. Gilse.—p. 1019.
Burns. I. Initial Treatment, Local and General. R. P. Osborne.—p. 1025.
Burns. II. Skin Cover for Full-Thickness Skin Loss. J. P. Reidy. —p. 1030.
Fixation of Corneal Graft by Acrylic Splint. H. B. Stallard.—p. 1034.
Effects of Penicillin and Streptomycin on Vaccine Lymph. V. N. Krishnamurthy.—p. 1035.

**Treatment of Rheumatoid Arthritis.**—Goslings and his associates of the University Hospital of Leyden, Holland, treated five patients with rheumatoid arthritis and one with ankylosing spondylitis with pituitary adrenocorticotropic hormone (ACTH). They used low dosage for two to six months. In three moderately severe cases of rheumatoid arthritis and in one serious case of ankylosing spondylitis the result was favorable. In two cases of rheumatoid arthritis with a complication (psoriasis, albuminuria) the improvement was temporary and relapse occurred in spite of a repetition of the initial high dosage. The condition of the four improved patients was maintained with 2 mg. of pituitary adrenocorticotropic hormone given six times daily. Reduction of the dosage to 1 mg. six times daily resulted in a relapse in three of these patients. An attempt was made to maintain their improved condition with gold therapy, but no conclusions can be drawn until more experience with this combined treatment is accumulated. The untoward reactions that are commonly observed after treatment with pituitary adrenocorticotropic hormone appeared in varying degrees of severity. A serious form of diabetes developed in one patient, who also showed symptoms of vascular occlusion. These phenomena gradually disappeared with a low dosage or after discontinuation of the hormone.

### Glasgow Medical Journal

31:315-370 (Oct.) 1950

*Simmonds' Disease: Report of Three Cases, with Particular Reference to Laboratory Diagnosis and Treatment. I. A. Anderson.—p. 315.
Case of Generalized Scleroderma Simulating Oesophageal Carcinoma. D. M. McClure.—p. 339.
Treatment of Varicose Veins of Lower Limb with Particular Reference to Location of Communicating Veins. R. B. Wright.—p. 351.
Case of Ball Thrombus of Heart. J. Fleming and B. Joels.—p. 360.

**Simmonds' Disease.**—According to Anderson, the following laboratory data are indicative of a diagnosis of hypopituitary cachexia (Simmonds' disease): (1) a low basal metabolic rate; (2) sensitivity to insulin as shown by the intravenous insulin tolerance test and the so-called "hypoglycemia unresponsive-

ness" (failure of the blood sugar to return to within 10 per cent of its fasting level in two hours after the intravenous injection of insulin); (3) a negligible urinary excretion of 17-ketosteroids; (4) a positive water test for adrenal insufficiency; (5) less essentially, subnormal levels of sodium and chloride in the serum and a subnormal urinary output of follicle-stimulating hormone. For the treatment of this disease, thyroid substance, desoxycorticosterone and testosterone are recommended. Case reports of three patients, two women and one man, given diagnoses of Simmonds' disease, are presented to illustrate the use of biochemical tests in diagnosis and the hormonal treatment of the disease.

## Medical Journal of Australia, Sydney

2:429-464 (Sept. 16) 1950. **Partial Index**

Some Aspects of Fat Metabolism. A. H. Ennor.—p. 432.
Errors Involved in Counting of Blood Cells. C. White.—p. 434.
Adrenals in Rheumatic Diseases. L. J. A. Parr.—p. 439.

2:465-496 (Sept. 23) 1950. **Partial Index**

Modern Trends in Diphtheria Prophylaxis. R. W. Patterson and E. A. North.—p. 470.
*Purified Toxoid Aluminium Phosphate ("P.T.A.P."): Report on Australian Field Trials. E. F. Mackenzie.—p. 473.
Pathogenesis of Atheroma with Special Reference to Disordered Lipoid Metabolism. G. V. Hall.—p. 475.

2:533-564 (Oct. 7) 1950

Essential Enuresis: Successful Treatment Based on Physiological Concepts. N. D. Crosby.—p. 533.
Tuberculosis at Brisbane Children's Hospital: Ten-Year Survey. F. Arden.—p. 543.
"Bad Risk" Anaesthetic in Emergency Surgery. A. L. Nathan and R. A. Joske.—p. 545.

**Purified Toxoid Aluminum Phosphate.**—Mackenzie reports a field trial carried out by the Victoria Department of Health, with purified toxoid aluminum phosphate (P.T.A.P.). Some 3,000 children were inoculated with one or more doses. This toxoid is easy to use, but like other toxoids it will give rise to reactions in the older age groups. Only four in every 1,000 children reported on had reactions that necessitated bed rest. Compared with the prophylactics in general use in Australia, namely, alum-precipitated toxoid and formol toxoid, purified toxoid aluminum phosphate does not cause local reactions as severe as alum-precipitated toxoid. The new toxoid will not necessitate as many injections as are required with formol toxoid. The general over-all conversion rate to a Schick-negative state in 1,550 children who received 0.75 milliliter of purified toxoid aluminum phosphate divided into two doses was 99.8 per cent. The following doses are recommended: for infants, a first dose of 0.25 milliliter subcutaneously administered and a second dose of 0.5 milliliter; school children, a first dose of 0.25 milliliter and a second dose of 0.5 milliliter, unless contraindicated, in which case the dose should be reduced to 0.25 milliliter or omitted. The interval between the two doses may be four to six weeks. Adults, students and persons previously inoculated should be submitted to Schick test. The Schick-positive persons should be given 0.25 milliliter doses. Boosting doses (0.25 milliliter for one injection) may be given as required for previously inoculated children entering school. Schick tests are not usually necessary except when one is dealing with persons mostly previously inoculated. The effectiveness of the new toxoid in controlling diphtheria will take time to prove. So far, the immunization procedure with purified toxoid aluminum phosphate has not failed in the presence of a virulent diphtheria organism in the community.

2:565-600 (Oct. 14) 1950

*Gastric Biopsy in Pernicious Anaemia. R. K. Doig and I. J. Wood.—p. 565.
Sarcoidosis: Survey, with Report of 30 Cases. B. Robinson and A. W. Pound.—p. 568.
Ocular Manifestations of Sarcoidosis with Description of Seven Cases. N. Lewis.—p. 582.

**Gastric Biopsy in Pernicious Anemia.**—Doig and Wood show that much information can be obtained in cases of pernicious anemia and in subacute combined degeneration of the cord by means of blind gastric biopsy. The biopsy is done with a flexible gastric tube, which consists of a length of Bowden wire covered by plastic tubing so that it is airtight. Attached to the distal end of the tube is a small metal cylinder containing a cylindrical knife. This knife can be moved up and down past a lateral hole by a long operating wire that protrudes from the upper end of the tube. The bottom end of the metal cylinder is sealed by a screw, which can readily be removed to obtain the biopsy fragment. Before the tube is passed, the patient is prepared by anesthesia of the throat with a cocaine spray and gargle and by emptying of the stomach. The biopsy tube is then gently inserted into the stomach to about 50 cm. Negative pressure is exerted with a hand pump connected to the upper end of the tube, and this sucks a knuckle of gastric mucosa into the lateral hole. This is cut off by upward action of the cylindrical knife. The patient experiences no pain when the mucosa is cut. After withdrawal of the biopsy tube the fragment is obtained by removal of the terminal screw and forcing out of the cylindrical knife. With this technic, 409 successful biopsies have been done on 345 patients. The authors were able to differentiate three types of diffuse change in the gastric mucosa—superficial gastritis, atrophic gastritis and gastric atrophy. Superficial gastritis and atrophic gastritis represent early and late stages of the one inflammatory process and are frequently associated with flatulent dyspepsia and achlorhydria. Gastric atrophy can usually be distinguished from chronic atrophic gastritis by the relative absence of inflammatory changes, the more complete nature of the atrophy and the greater incidence of intestinal metaplasia of the epithelium. Gastric atrophy is almost invariably accompanied with pernicious anemia or subacute combined degeneration of the cord, and these diseases are rarely present in its absence. Gastric atrophy is not affected by adequate treatment with liver extract. Gastric biopsy could be helpful in the diagnosis of pernicious anemia when liver therapy has been given without an adequate hematological examination.

## Acta Radiologica, Stockholm

34:1-144 (July-Aug.) 1950. **Partial Index**

*Influence of Blood Pressure in Urographic Examination (Preliminary Report). I. Wickbom.—p. 1.
Fibro-Osteoma in Mandible of Child. A. Sonesson.—p. 17.
Intraosseous Mucus-Secreting and Cystic Epidermoid Carcinoma of Jaw. A. Sonesson.—p. 25.
Estrogen Therapy in Prostatic Carcinoma. P. E. Andersen.—p. 33.
Osseous Changes in Neural Leprosy: Radiological Findings. J. Barnetson.—p. 47.
Thoracic Aortography in Diagnosis of Patent Ductus Arteriosus Botalli. B. Broden, G. Jönsson and J. Karnell.—p. 65.
Calcification of Vasa Deferentia. P. E. Andersen.—p. 89.
*Further Experimental Investigations of Injuries from Contrast Media in Cerebral Angiography: Summation of Various Injurious Factors. T. Broman, B. Forssman and O. Olsson.—p. 135.

**Blood Pressure in Urographic Examination.**—Intravenous urography makes it possible to study not only the anatomy of the renal pelvis, but also the physiology of the kidney. In the study of the function of the kidney, the fluid balance of the patient and the blood pressure have to be considered. Wickbom reports on two cases in which the systolic blood pressure fell to 70 mm. of mercury or less following intravenous injection of the contrast medium. As long as the blood pressure was low, no secretion of contrast material took place, but when the blood pressure was raised by the injection of ephedrine, contrast medium was excreted into the renal pelvis. Therefore, if urography gives unsatisfactory results, it should be remembered that a fall in blood pressure may be responsible.

**Injurious Effects of Cerebral Angiography.**—Broman and associates performed animal experiments to determine whether the technic of injection or the presence of vascular disease increased the risk of damage to the cerebral vessels in cerebral angiography with contrast media of the iodopyracet injection (diodrast®) type. They found that repeated injection of a contrast medium into the carotid artery involves the risk of a summation effect if the interval between the individual injections is short. Even slightly toxic media are injurious if injected in this manner. If the blood circulation of even a part of the brain is retarded, the resulting prolongation of application of the contrast medium is likely to lead to injury, even if the contrast medium is injected fairly rapidly. Latent vascular injury in the brain is likely to be aggravated and become manifest by the injection of a con-

trast medium of the iodopyracet injection type in cerebral angiography. This was demonstrated exerimentally by injection of another chemotoxic substance in an otherwise noninjurious quantity immediately before, or simultaneously with, the injection of the contrast solution. Certain cerebral disease processes may presumably be affected similarly.

## Deutsche medizinische Wochenschrift, Stuttgart

75:1277-1316 (Sept. 29) 1950. Partial Index

*Triad of Fever, Erythrocyte Sedimentation Rate and Deviation to the Left in Evaluation of Chemotherapeutics in Tuberculosis. A. Westergren.—p. 1277.
*Prognostic Evaluation of Tuberculous Infection. H. Kleinschmidt.—p. 1280.
Roentgen Irradiation of Residual Tuberculous Cavities After Thoracoplasty. H. Deist.—p. 1285.
Prophylaxis and Therapy of Poliomyelitis. H. Pette and R. C. Behrend.—p. 1288.

**Evaluation of Chemotherapeutics in Tuberculosis.**—Since 1944 about 600 tuberculous patients in Stockholm have been treated with various new drugs, including the sulfones, paraaminosalicylic acid, streptomycin and the thiosemicarbazones. These drugs were first used alone and later in combinations of two or more. The author's simplified method of studying their effects consisted in determination of the temperature, sedimentation rate and number of immature neutrophils during a preliminary period and again after treatment with a certain drug or combination of drugs. The result was considered good when, after 30 days, there was a noticeable improvement in temperature, a decrease in sedimentation rate and in the number of immature neutrophils. Each of these changes signifies different reactions, which, on the whole, take a parallel course but also show some independent development. The disparities may furnish important clinical information; for instance, patients exclusively treated with streptomycin show an improvement in the deviation to the left more often than do those treated with paraaminosalicylic acid, whereas in patients treated with this latter drug modification of the sedimentation reaction is more noticeable. Such disparities indicate that the different drugs have different points of attack, and they also argue in favor of the combined use of two or more drugs.

**Prognostic Evaluation of Tuberculosis Infection.**—According to Kleinschmidt, the prognosis of asymptomatic primary tuberculosis infection, while usually good, is always uncertain and difficult to judge. The available prognostic tests are inadequate. Repeated roentgenologic examinations and determination of erythrocyte sedimentation rate, tuberculin titer and type and virulence of the bacillus are not always reliable indications of the future course of the disease. Even observation of the patient's constitutional type, formerly stressed, gives little information. Contrary to previous belief, it has been shown that children with exudative-lymphatic diathesis are not more susceptible to the development of tuberculous meningitis. Rather, they seem to tolerate tuberculosis infection better than other children. The author cites observations, however, that indicate that the time relation between local infection and dissemination is of great importance for prognosis. The greatest danger exists during the first year after infection. If the time of infection can be ascertained by history of exposure to an infected person or conversion of the tuberculin reaction from negative to positive, special measures to increase the resistance should be taken for about a year thereafter.

## Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

94:2785-2884 (Sept. 30) 1950. Partial Index

Diagnosis and Treatment of Blockage of Nose Caused by Insufficiency of Vestibulum Nasi. G. J. Smelt.—p. 2792.
Clinical Symptoms Caused by Double Aortic Arch. J. Exalto, W. K. Dicke and W. C. Aalsmeer.—p. 2798.
*Treatment of Skin Disorders with Undiluted Tar. J. C. M. Grosfeld.—p. 2804.

**Undiluted Tar in Treatment of Skin Diseases.**—Grosfeld applies undiluted tar to skin lesions with a spatula. A thick layer is applied and then dried with an electric dryer. Tar is applied for five successive days, wherever the first layer has become detached. After the fifth day, the tar is no longer replaced, and it becomes entirely detached in two or three days. If the therapeutic result is not satisfactory, the treatment can be repeated after three to five days. Rapid cessation of itching, a drying effect on exudative processes and rapid reduction in hyperemia in the congestive processes are the chief effects obtained. The authors used this therapy in about 40 cases of various types of eczema and in a few cases of psoriasis, erythrodermia and prurigo Besnier. In the patient with erythrodermia, the tar produced irritation and the treatment had to be discontinued. The girl who had Besnier's prurigo was relieved only of the itching, but otherwise her skin lesion remained unchanged. The four patients with psoriasis responded favorably at first but had recurrences. Various forms of eczema responded favorably to treatment with tar. The author believes that there are no cancerigenic effects of tar therapy. The development of hypersensitivity to tar was investigated in 35 of the patients who had been treated. It was found that seven had a hypersensitivity, but the reactions were never severe.

## Nordisk Medicin, Stockholm

44:1553-1586 (Sept. 29) 1950

Antibiotics. Experimental Background and Clinical Application. P. H. Long, E. A. Bliss, E. B. Schoenbach and others.—p. 1553.
*Pharmacoradiography of Stomach. T. Rasmussen.—p. 1563.
Chronic Pancreatitis: Pancreatic Calcification, Diabetes and Steatorrhea. S. Aarseth.—p. 1567.
*Course of Pregnancy in Diabetes. J. Möllerström.—p. 1570.
Undulant Fever Treated with Aureomycin. J. Røjel.—p. 1573.
Interstitial Pregnancy. C. Rindom-Schiøtt.—p. 1572.

**Pharmacoradiography of Stomach.**—Rasmussen, who has previously reported on pharmacoradiography of the stomach with morphine and ipecac, now reviews the results of continued investigations with other drugs. The object of the study is to find the drug that best facilitates examination of the stomach by increasing tonus and peristalsis when diagnosis is made difficult by atonia, failure of peristalsis, stenosis or infiltrations with uncertain dimensions. Morphine citrate given intravenously produced the desired effect but caused troublesome side effects. A combination of 6 mg. of atropine sulfate and 0.5 mg. of neostigmine in the same syringe, injected subcutaneously, was found to be most suitable for the purpose. Tonus and peristalsis were increased in almost all patients examined; dilatation of the bulb resulted in better filling and better passage through pylorus, and there were no side effects.

**Course of Pregnancy in Diabetes.**—Möllerström followed the course of 98 pregnancies in 46 diabetic women. Forty-two had severe diabetes and received up to 80 international units of insulin daily; four had mild diabetes. There were 12 abortions in or before the fifth month, 80 full term deliveries with 37 live births, 40 stillbirths and three twin pregnancies with one living fetus. Cesarian section was done in six additional cases, with five live births. In cases where the start of the diabetes coincided with the pregnancy, the fetal mortality was slight, but when pregnancy occurred after the onset of diabetes there was a noticeable reduction in fetal viability. The mother's age seemed to play no part in determining the viability of the fetus. In 1949 all but one of 34 surviving children (aged from 1 to 23) born to mothers with severe diabetes were well; one child aged 13 had had diabetes since she was four.

## Presse Médicale, Paris

58:1285-1300 (Nov. 18) 1950

Syndrome of Isolated Thrombosis of Anterior Tibial Artery and Its Treatment. R. Leriche.—p. 1285.
*Febrile Reactions to Paraaminosalylic Acid (PAS). B. Kreis, A. Libert, F. Paquelin and J. Abric.—p. 1285.
New Technical Procedure in Insulin Shock. B. Yagdjoglou.—p. 1287.

**Febrile Reactions to Paraaminosalicylic Acid.**—Kreis and co-workers report the occurrence of febrile reactions to paraaminosalicylic acid in eight tuberculous patients receiving 10 to 18 Gm. of the drug per day. An isolated sudden rise of temperature up to 104 F. occurred in three patients, suggesting erroneously the development of severe complications. Fever with impressive oscillations occurred in two patients. Progressive rise of temperature in the course of several days up to 104 F. was observed in two other patients, suggesting acute dissemina-

tion. Rise of temperature was associated with a morbilliform erythema and lasted for 11 days in one patient. These reactions occurred in patients of both sexes, with various forms of tuberculosis. The reactions occurred between the eighth and thirty-eighth day of the treatment after the ingestion of 80 to 608 Gm. of the drug. The amount of the daily dose does not seem to have been a determining factor. The fever responded to antipyretics, but the essential factor in diagnosis was the sudden and definite drop in temperature as soon as the paraaminosalicylic acid was discontinued. Immediate rise of temperature after readministration of the drug provided definite proof that the drug was the exciting factor. These febrile reactions showed intolerance to paraaminosalicylic acid.

## Revista Brasileira de Tuberculose, Rio de Janeiro

**18:**117-190 (March-April) 1950. **Partial Index**

*Dried BCG Cultures. D. M. Cardoso and W. F. Almeida.—p. 119.

**Dried BCG Cultures.**—Cardoso and Almeida describe their technic of lyophilizing BCG cultures in large quantities for use in vaccination. They used the Stokes lyophilizing chamber, the temperature of which is adjustable between —40 C. and + 50 C. The bacterial suspension is frozen in the chamber, and water is evaporated by high vacuum, while the temperature is maintained below 0 C. The best results, with respect to survival of living organisms, were obtained when the temperature of the chamber at the beginning of the procedure was —28 C. The high vacuum was established after the suspensions were frozen, maintained in the presence of a constant temperature of —6 C. until the material was completely dried and then replaced with filtered air. The whole process required 18 hours. In preparation of bacillary suspensions to be dried, human plasma, horse serum and skimmed milk can be used as suspension liquids with good results. Solutions of dextrose and lactose are poor mediums, because they are difficult to dry and because of the coarseness of the suspension obtained with the dried material. Forty-four per cent fewer BCG colonies were obtained from dried cultures than from nondried cultures prepared with the same amount of BCG suspension. The total weight of the colonies produced by the dried cultures and by the control cultures, was about the same. The antigenic properties and harmlessness of BCG cultures were not altered by the lyophilizing process.

## Semaine des Hôpitaux de Paris

**26:**4107-4140 (Oct. 26) 1950. **Partial Index**

*General Remarks on 300 Cases of Typhoid Fever Treated with Chloramphenicol (Chloromycetin®) Combined with Other Antibiotics. E. Benhamou, F. Destaing and A. Sorrel.—p. 4107.
Problem of Surgical Treatment of Intestinal Perforations Associated with Typhoid Fever. E. Benhamou, L. Cohen-Solal and R. Le Go. —p. 4109.
Typhoid Myocarditis and Its Electrocardiographic Control. E. Benhamou and E. Albou.—p. 4115.

**Chloramphenicol (Chloromycetin®) in Typhoid Fever.**—Benhamou and co-workers treated 300 patients with typhoid and paratyphoid fever with chloramphenicol (chloromycetin®). Complete recovery occurred in 86 of the first 100 patients, in 94 of the next 100 and in 98 of the last 100 patients. The progressive increase in the recovery rate was due to immediate institution of treatment as soon as the clinical diagnosis of typhoid fever was made and to combined administration of chloramphenicol, other antibiotics and antitoxins. Common forms of typhoid and paratyphoid fever were found in 241 patients, and 59 had malignant forms. In adults with moderate symptoms chloramphenicol in doses of 3 Gm. daily (0.25 Gm. every two hours) proved effective. In severe forms of the disease an initial massive dose may be indicated. Of the last 100 patients, 22 were given chloramphenicol in doses of 1.5 Gm. twice daily. Apyrexia was thus obtained in adults within three to four days. In children, chloramphenicol suppositories (0.25 Gm.), administered two or three times daily proved satisfactory. There were 14 recurrences in the first 100 cases, 12 recurrences in the next 100 and only five in the last 100. This improvement was due to continuation of chloramphenicol in smaller doses for two weeks after apyrexia was obtained. In the malignant cases of the disease the authors recommend treatment with an antibiotic mixture consisting of chloramphenicol, aureomycin and streptomycin. Along with this they give convalescent globulins and serum obtained from hyperimmunized animals.

## Wiener klinische Wochenschrift, Vienna

**62:**765-784 (Oct. 13) 1950. **Partial Index**

Perception as Nervous Function. G. Schubert.—p. 765.
Nature and Pathogenesis of Infectious Diseases. H. Zischinsky.—p. 767.
*Persistence of Antibodies Against Rhesus Factor in Serum of Immunized Persons. P. Speiser and J. Schwarz.—p. 770.
Electrophoretic Examination of Blood Plasma in Relation to Problem of Aging of Preserved Blood. W. Auerswald and M. Wenzl.—p. 775.

**Persistence of Anti-Rh Agglutinins in Serum of Sensitized Persons.**—Speiser and Schwarz studied the development and persistence of anti-Rh agglutinins in the serum of 60 persons (four men and 56 women) who had been sensitized by an Rh-positive transfusion or an Rh-positive fetus. The interval between sensitization and first determination of antibody titer varied from six weeks to 38 years. Subsequent periodic serologic examinations were carried out for from one to 24 months. In no case could complete disappearance of antibodies be demonstrated. Two young men maintained titers of anti-Rh agglutinins in spite of frequent donations of blood amounting to 19 liters in 33 months. They reformed antibodies more rapidly than hemoglobin. It was apparent that all these patients had become actively immunized against the Rh factor and that antibody formation had become self perpetuating. Five instances of passive immunization with Rh antibodies were also observed.

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Experimental Autoinfection. N. Anitschkow.—p. 785.
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Different Effect of Methylphenylethylhydantoin (Mesantoin) in Attacks of Epileptic Convulsions and Tetany Spasms. H. Jesserer.—p. 787.
*Additional Results of Treatment with Streptomycin in Disseminated Forms of Tuberculosis. O. Ruziczka.—p. 791.

**Streptomycin in Disseminated Forms of Tuberculosis.**—Ruziczka reports on 22 children with miliary pulmonary tuberculosis, six with tuberculous peritonitis and 110 children with tuberculous meningitis who were treated with streptomycin. All the children with miliary pulmonary tuberculosis have been followed for at least six months since treatment was started. One cachectic infant died in the fifth week of the treatment; one child showed meningeal symptoms on the seventh day of treatment, so that meningeal dissemination may have occurred before the institution of the treatment. Meningitis appeared immediately after the institution of treatment in two children and occurred two weeks after a three month course of streptomycin in a fifth patient. Miliary changes could no longer be demonstrated on roentgenologic examination in the remaining 17 children after two and a half to five months of treatment with streptomycin. Treatment has been discontinued for two years in some of these children, and all of them have remained free of complaints. Five of the six children with tuberculous peritonitis responded satisfactorily and rapidly to streptomycin therapy. Defervescence occurred within a few days, and ascites subsided without puncture. One cachectic infant with severe ulcerative intestinal tuberculosis and peritoneal tuberculosis died despite treatment with streptomycin. Results showed that prognosis of miliary pulmonary tuberculosis and tuberculous peritonitis treated with streptomycin is favorable. Of the 110 children with tuberculous meningitis, who were admitted to the hospital for streptomycin treatment up to June 30, 1950, 41 were discharged as clinically recovered, 12 are still under treatmen and 54 have died. Seventy-eight of the 110 children have been followed for at least 12 months since treatment was started. Of these, 32 were discharged as clinically recovered, treatment still continues in one and 45 have died. There was an increased incidence of tuberculous meningitis and a poorer prognosis in the patients aged less than 3 years. Early diagnosis is still difficult, but the possibility of tuberculous meningitis always should be considered, particularly in tuberculin-positive infants with an obscure febrile condition, so that the first precious days of streptomycin therapy will not be lost.

# BOOK REVIEWS

**United States Civil Defense.** Executive Office of the President, National Security Resources Board, NSRB Doc. 128. Paper. 25 cents. Pp. 162. Superintendent of Documents, Government Printing Office, Washington 25, D. C., 1950.

The greatest deterrent to a sudden and devastating attack on the United States is the power to destroy an aggressor by retaliatory action. An effective civil defense is therefore vital because it would enable the people, if heavily attacked without warning, to recover and to fight back. Although an enemy would presumably attack metropolitan areas and other critical targets, he would in reality be attacking all the people of the United States at the same time, and defense against his efforts would require the coordinated effort of the whole nation. An attack of this nature would be partially successful, since military defense can never be absolute, but whether it would destroy the industrial capacity that has decided two world wars would depend mainly on the efficiency of our civil defense—a vital element that must take its place along with military defense if the national security structure of the United States is to be complete.

This report, which utilizes the wartime experiences of Great Britain and Germany as well as previous planning undertaken by agencies of the United States government, provides an outline of the organization and procedures that should be developed by the states and local communities, who are primarily responsible for organizing and training the many types of specialized groups that would be required to cope with the devastating effects of modern weapons. The report defines civil defense as "the protection of the home front by civilians acting under civil authority to minimize casualties and war damage and preserve maximum civilian support of the war effort" and declares that "the basic operating responsibility for civil defense is in the individual and his local government. The individual, given all training possible, does what he can for himself in an emergency. The family unit, similarly trained, attacks its own problems while also contributing to the organized community effort. The community's civil-defense organization works to meet its own crisis, receiving outside help if its facilities are inadequate, or contributing support to neighboring communities under organized State direction. In order to help communities carry out their responsibility, the State and Federal Governments contribute assistance in organizational advice, over-all planning, and resources."

The suggested over-all policy, the basic concepts and the basic responsibilities of civil defense are first presented, after which there is an enumeration and description of the services necessary for operation of the specific civil defense functions. Finally, there are suggestions for the actual initiation of civil defense programs by the states and communities. The section on civil defense health and medical services describes these in functional rather than organizational units, since no single organizational blueprint could be applied equally to every state or community. This section will be supplemented within the near future by manuals that will cover the required specific technical information more thoroughly than was possible within this report. The civil defense health and medical services would be responsible not only for the relief of suffering and the provision of emergency life-saving measures after a civilian wartime disaster but for the preservation or restoration of the health services that exist normally during peacetime. In addition, and since the effects as well as the detection of atomic, biologic and chemical warefare agents are such that defense against them should be supervised by trained health personnel, the basic responsibility for defense measures against these special weapons is assigned to the health services, with other services participating wherever their functions are involved.

The report recommends that the state health officer be placed in charge of all state civil defense health and medical services and that cities appoint local health officers in the same manner, so that existing health agencies may be utilized and the creation of new and duplicating agencies may be avoided. The report also recommends that each state establish a civil defense advisory council and that this include representatives of each of the major professional health organizations within the state. Expert professional advice and assistance would thus be available to those responsible for planning, organizing and directing the civil defense programs of the states and communities.

**Facts of Life and Love for Teenagers.** By Evelyn Millis Duvall, Ph.D., Consultant, National Council on Family Relations, Chicago. Cloth. $3. Pp. 360, with illustrations. Association Press, 291 Broadway, New York 7, 1950.

In all books of this nature, the backgound, fluency and understanding of the author are the most important factors in an evaluation of the volume. The author writes with authority because of her extensive experience in the field of counseling, and her literary approach is refreshingly frank and explanatory. There is ample evidence that considerable research and study have gone into preparation of the book.

The volume is arranged in four parts. The first part is an instructive discussion of the anatomy and physiology of sex and pregnancy. Also considered are subjects such as homosexuality, masturbation, venereal disease and sexual adjustment. This part is generously interspersed with reproductions from the outstanding exhibit of the Chicago Museum of Science and Industry on pregnancy and birth. It would have been helpful, however, for the author to have emphasized the importance of avoidance of transfusion of Rh-negative females of all ages, even in childhood, with Rh-positive blood, since this is a precaution often overlooked. Titles of the pregnancy tests described have been reversed, but this is a technical matter that is of little real importance. Remaining sections of the volume deal principally with problems of social adjustment, one going extensively into the matter of dates (which parents will read with interest), another with love, petting and the extremes that should be avoided and the final section with preparation for marriage. There is much sensible, matter-of-fact material in this last section, with especially good advice on sex adjustment and premarital examinations.

In addition to the special reproductions already mentioned, the book is attractively illustrated with full page and marginal sketches that give emphasis to points in the text. This book may be recommended by physicians for adolescent reading. Many parents, including physician parents, would do well to read it first themselves.

**Patologia, parassitologia ed igiene dei paesi caldi.** Dal Prof. Mario Giordano, T. generale medico della Marina militare, direttore generale della sanità M. M., Roma. Volumi I e II. Third edition. Cloth. 12000 lire. Pp. 812; 815-1627, with 598 illustrations. L. Cappelli, Via Farini, 6, Bologna, 1950.

In a lengthy preface the author of this treatise on tropical pathology and public health comments on the notable progress in applied therapy and prophylaxis that has occurred in the past decade and enables the peoples in warm climates to develop better ways of life. Intimate knowledge of many of the diseases of man and domestic animals has been acquired by Dr. Giordano from his years of experience as a medical officer of the Italian Government in Somaliland and other former Italian colonies.

The subject matter is divided into 12 parts: rationale of tropical hygiene, tropical diseases of protozoan, spirochetal and rickettsial origin, helminthic infections, arthropods in relation to disease, animal and plant intoxicants and venoms, bacterial diseases, deficiency diseases, mycoses, viral diseases, psychotic and nervous ailments of warm countries, taxidermy and embalming together with preservation of anatomical specimens and international and national sanitary codes. There is an exhaustive subject index. Although the reader may disagree

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

with the author on the appropriate sequence of subject groups, one admires the comprehensive way in which this herculean task has been undertaken and the meticulous care which has been given to detail regardless of the subject.

The reviewer was impressed by the wealth of valuable information in the chapters, the accuracy in designation of etiological agents, the objectivity of the historical statements and the modern viewpoint with reference to therapy and control. Perhaps the author could have improved some of the chapters by abbreviating the older therapeutic procedures and placing greater emphasis on the more effective recent drugs and antibiotics.

One of the assets of this work is the abundance of excellent clinical photographs and photomicrographs, which are well produced. On the whole, the numerous line and stipple, halftone drawings and color plates are much less impressive. One of the deficiencies of the work is almost complete failure of the author to cite authorities. This undoubtedly explains the absence of an author index. Moreover, three of the maps on the distribution of disease are inaccurate. Pages 1625-1627 provide a list of pharmaceutical and biological firms in Italy and the therapeutic drugs referred to in the text (with page references) which can be purchased from each firm.

The pages are large octavo, of good quality paper and excellent type. The volumes are substantially and attractively bound in cloth. Although this treatise on tropical medicine is intended primarily for Italian physicians practicing clinical and public health medicine in Africa, it will be welcomed by all who are concerned with diseases and their control in warm climates.

**The Development of the Human Eye.** By Ida Mann, M.A., D.Sc., M.B., Surgeon, Moorfields Eye Hospital, London. With a foreword to the first edition by Sir John Herbert Parsons, C.B.E., F.R.S., D.Sc. Second edition. Cloth. $6.50. Pp. 312, with 239 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1950.

The publication in 1928 of the first edition of this fundamental work on the development of the human eye established the author as the leading authority on ocular embryology, a reputation she has since continued to enjoy. Unfortunately, the book has been unobtainable for a number of years. The appearance of this edition is therefore to be welcomed as filling a much needed place in the ophthalmological literature. Since knowledge of embryology has changed but little since the appearance of the first edition, only minor additions and changes have been introduced in the present edition, but the author has made an excellent attempt to bring all information on the subject up to date.

While textbooks on anatomy or embryology, being based on detailed factual material, cannot make light or easy reading, Miss Mann does well in expressing herself clearly and intelligibly. There are adequate illustrations. To the clinical ophthalmologist, the most vitally interesting chapters are those on congenital anomalies and on the synoptic comparison of ocular with general developments, where developmental features are considered in readily available tabular form. This book makes available a reference book on embryology of the eye that is complete and authoritative. It should be in the library of every ophthalmologist who does not possess the first edition and should be available to every student of embryology.

**Lehrbuch der Chirurgie. Band II.** Herausgegeben von A. Brunner, et al. Unter Mitarbeit von F. Becker, et al. Cloth. 76 Swiss francs. Pp. 913-2037, with 448 illustrations. Benno Schwabe & Co., Klosterberg 27, Basel 10; Imported by Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1950.

This is a work on general surgery written by a group of Swiss authors in German. The subjects considered are surgery of the face and oral cavity, the neck, thymus, esophagus, thorax, breast, abdominal wall and alimentary canal, liver, bile passages, pancreas, spleen, abdominal surgery of infancy and childhood, hernias, vertebral column and pelvis, kidney, bladder and male genitalia (gynecology is omitted), extremities, orthopedics (for the general practitioner), prostheses, traumatic surgery and the anatomicophysiology of the sympathetic nervous system. The information presented is classical, and due cognizance is taken of recent advances in all the branches of surgery considered. The work seems to be directed principally to students, internes and residents, although it may serve well as a ready reference book in broad terms for general practitioners. Details of operative technic, results of treatment and the bibliography are not given in a satisfactory manner for the surgical specialist. The illustrations are very numerous and excellent. Drawings, photographs and charts are well reproduced. The quality of paper is excellent; the typography is perhaps one of the most outstanding features of the work. Unfortunately the book is written in German, and this will limit its demand in this country. For the reader who is proficient in German, the text is as good a reference for surgical principles as has been published in recent years.

**Regional Orthopedic Surgery.** By Paul C. Colonna, Professor of Orthopedic Surgery, University of Pennsylvania Medical School, Philadelphia. Cloth. $11.50. Pp. 706, with 474 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1950.

Dr. Paul C. Colonna received much of his orthopedic training under the tutelage of one of the first great American orthopedic surgeons, Dr. Royal Whitman. The influence of Whitman, who was only satisfied with the best, and who was never patient with mediocrity, was reflected by Dr. Colonna at the University of Oklahoma where he served as Professor of Orthopedic Surgery before he assumed his present position. Throughout his professional career Paul Colonna has been a teacher. As he states in the preface to this book, he has found it advantageous to present the study of orthopedics to both graduate and undergraduate students from a regional approach, which is also used in this newest of a number of recently published books dealing with the problems of the orthopedic surgeon, diagnoses and clinical management. This book begins with a discussion of the physiology of bones and joints and contains a very careful description of the orthopedic examination, including muscle function testing. Surgical technics and other forms of orthopedic therapy are discussed briefly and without the benefit of as many illustrations as might be desirable. However, this book emphasizes a point of greatest importance to the student, whether undergraduate or graduate, namely, a more thorough understanding of the nature of the conditions that produce crippling and the procedures in accurate diagnoses.

**Thoracic Surgery.** By Richard H. Sweet, M.D., Associate Clinical Professor of Surgery, Harvard University Medical School, Boston. Cloth. $10. Pp. 345, with 155 illustrations by Jorge Rodriguez Arroyo, M.D., Assistant in Surgical Therapeutics, University of Mexico Medical School. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1950.

This book is divided into 11 chapters arranged in the following order: surgical anatomy of the thorax, general technical considerations, thoracic incisions, operations on the thoracic wall, operations concerning the pleural cavity, operations on the lung, operations within the mediastinum and operations on the esophagus.

It is indeed refreshing in this day of superspecialization to read in the preface of Dr. Sweet's book: "The wide scope of the material presented necessitates the description of procedures which involve a familiarity not only with the thorax but also with the neck and abdomen. This fact serves to illustrate the oneness of all surgery and to emphasize the concept that competence in the special field of thoracic surgery demands a thorough familiarity with the surgery of these other regions as well."

The first chapter, which pertains to surgical anatomy, is well written. Despite its brevity it is quite inclusive. The technical procedures, whether the relatively simple thoracotomy or the massive esophageal resections, have all received their proper importance. On page 164, the step by step outline of procedures is presented. These include pneumonectomy, upper and middle lobectomy, lingulectomy and lower lobectomy. Such outlines have a place if the over-all subject is properly presented.

In the treatment of idiopathic dilatation of the esophagus (achalasia), the author prefers to correct the condition by a

longitudinal incision with a circumferential closure through a transthoracic approach. He describes this as the most effective method. Although the Heller operation is mentioned by Dr. Sweet, a little more space could have been devoted to this latter procedure, since its results have also been uniformly good.

The subject of heart surgery is also given its proper importance in this work. The very timely approach to abdominal operations through thoracic incisions is discussed, and in this section gastric surgery, splenectomy, adrenalectomy, nephrectomy and portacaval anastomoses are described.

It is unfortunate that the illustrations are not of the same fine caliber as the text. In many of the drawings it is difficult to become oriented, and the sense of third dimensional view is almost entirely lacking. The book is well written, and the reader is impressed with the tone of authority that can only come from the vast practical experience that Dr. Sweet has had. This book can be highly recommended.

**Therapeutic Radiology.** By George Winslow Holmes, M.D., Radiologist, Waldo County General Hospital, Belfast, Maine, and Milford D. Schulz, M.D., Radiologist, Massachusetts General Hospital, Boston. Cloth. $7.50. Pp. 347, with 121 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1950.

The quality of the material presented in this book is attested to by the fact that the editor is one of the most experienced physicians in the use of radiation methods for the management of malignant diseases and by the fact that he has selected as authors a group of outstanding physicians with years of experience in this field. The physical and biologic basis of radiation therapy is presented by writers of equal competence. The clinical material is arranged under the various anatomic regions where the primary growths appear. The problems of classification, pathology, diagnosis and differential diagnosis of neoplastic diseases are well presented. The text includes chapters on special technics, such as supervoltage therapy and radioactive isotopes for both therapeutic and diagnostic purposes, and discussions of the use of hormones in neoplastic diseases and of the care of patients receiving intensive radiation. The last of the 40 chapters presents a list of books on technical phases of radiation therapy, history, physics and biophysics. The book is generously illustrated and the reproductions of roentgenograms are good.

It is probable that some workers may disagree with some of the technics presented by these writers and also with some of the statements and conclusions as to indications for and results of radiation therapy. However, this book contains much important, concentrated information. It will serve as a basic textbook for the younger and as a reference work for the older workers in this field.

**Los Angeles County Hospital House Staff Manual.** David Hamm, Jr., M.D., Editor-in-chief, Raymond D. Goodman, M.D., Ernest T. Smith, M.D., and Robert H. Van Scoyoc, M.D., assistant editors. Sixth edition. Looseleaf. Boards. Pp. 507. Los Angeles County General Hospital, Room 1042, 1200 N. State St., Los Angeles 33, 1950.

The primary purpose of this book is the education and guidance of the house staff of the Los Angeles County Hospital. It is full of useful, concise information on all subjects of immediate practical value to a resident hospital staff. It is really astounding that so much information can be contained in a volume of this size. All phases of medicine are covered including general medicine, general surgery, urology, orthopedics, gynecology, obstetrics, dermatology. Comprehensive instruction is given in the many diagnostic and therapeutic procedures used in a modern hospital today. The information is up-to-date and authoritative. The common laboratory procedures are outlined together with the indications for their use. There are new chapters in this edition on body fluid and electrolyte balance, anticoagulant therapy, immediate management of the unconscious patient and medicolegal briefs. The commonly used drugs and prescriptions from the hospital formulary are given as well as a list of drugs requiring special forms because of federal or state laws or hospital rules. This house staff manual can well serve as a ready reference book for house staff members of other hospitals and the busy general practitioner.

**Child Psychiatry in the Community: A Primer for Teachers, Nurses, and Others Who Care for Children.** By Harold A. Greenberg, M.D., Senior Staff Psychiatrist, Institute for Juvenile Research, Chicago. In collaboration with Julian H. Pathman, Ph.D., Chief Psychologist, Downey Veterans Administration Hospital, Downey, Illinois, Helen A. Sutton, R.N., B.A., B.S., and Marjorie M. Browne, B.A., M.A. Cloth. $3.50. Pp. 296. G. P. Putnam's Sons, 2 W. 45th St., New York 19, 1950.

Production of this volume by a team of specialists has had undeniably good results. A blending of the many different approaches necessary for adequate understanding of child guidance has been accomplished. Impressive evidence is presented that this sort of teamwork can be developed at local levels everywhere, and the book serves as an excellent guide to workers in this important field and provides understanding and appreciation of the general subject. There is a refreshing absence of any tendency to imply that psychiatry is the only adequate approach to solution of the problems of childhood. As the introduction states, it is important that parents develop more understanding and appreciation of child guidance clinics, but at the same time such clinics still are far short of what they may be expected ultimately to accomplish.

The book is divided into three sections that fall into a natural sequence. In the first section, the child is considered; included in these seven chapters are the psychogenesis of behavior problems, symptoms, diagnosis and treatment. In the second part, the clinic team, consisting of psychiatrist, psychologist and social workers, is described with details of the part played by each. Numerous psychological tests are listed, and qualifications and activities of the social worker are detailed. The final section is concerned with integration of the child guidance clinic into other community activities and services. Throughout the book, specific examples illustrate the discussion. An appendix contains data on services of the Psychiatric Department of the Cook County (Chicago) Juvenile Court, with reproductions of forms employed. There are a three-page glossary and an extensive list of suggested readings. This volume gives a timely and valuable survey of a much needed service that is undergoing extensive development.

**Tuberculosis and Other Problems of Pediatrics.** By Arvid Wallgren, M.D., Professor of Pediatrics, The Royal Caroline Medical Institute, Stockholm, Sweden. The Abraham Flexner Lectures, Series Number 10. Cloth. $2.25. Pp. 108, with 7 illustrations. Published for Vanderbilt University by The Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1950.

This volume is the tenth in this series of lectures delivered at the School of Medicine of Vanderbilt University and is a good example of the general excellence of the series. The author is especially qualified to deal with each of his subjects. The chapter on tuberculosis control is a lucid summary of public health facilities and activities in Sweden. The results of these activities, as reflected by the present low mortality rate, are commendable. The chapter on BCG vaccination should be of particular interest to American physicians. It is brief and authoritative and surveys all that has been learned about BCG in Sweden during the last 25 years. Dr. Wallgren's remarks on erythema nodosum and infantile hypertrophic pyloric stenosis will be of interest to all clinicians, and comments on the illegitimate child in Sweden have a wide general appeal to all those concerned with social pathology. This book is highly recommended.

**Physiology and Anatomy.** By Esther M. Greisheimer, M.A., Ph.D., M.D., Professor of Physiology, Temple University School of Medicine, Philadelphia. Sixth edition. Cloth. $4. Pp. 841, with 478 illustrations. J. B. Lippincott Company, 227-231 S. 6th St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1950.

This attractively bound and richly illustrated textbook is intended for use in training schools for nurses where anatomy and physiology are given as a combined course. The material from previous editions has evidently been repeatedly examined and has acquired the smoothness and authority that can come only from long years of use in actual teaching. Especially well-written, though not yet cleared of slight pedagogic flaws, is the interesting new material on aviation physiology from the nurse's viewpoint. This book can be highly recommended to the readers for whom it is intended.

# QUERIES AND MINOR NOTES

## TELEVISION

To the Editor:—*Kindly give me an opinion on the optimal distance from which to watch television? Is there any formula by which one may compute the optimal distance to watch a television screen of a given size? I have read several conflicting opinions on this subject. The American Society for the Prevention of Blindness states that one should not watch television from a distance less than 10 times the diameter of the television tube. If this is so, many persons are jeopardizing their sight, as most television sets are too large for their living rooms.*

*William Blake, M.D., Astoria, L. I., N. Y.*

This inquiry was referred to three authorities, whose respective replies follow.—Ed.

Answer.—When television is viewed from a distance less than 10 times the diameter of the television tube, no harm whatever is done to the eyes but the picture loses in quality, as the scanning lines then become visible. Great Britain and France are using a scanning level of 405 lines, but the United States about 500 and the USSR 625 lines, which shows signs of becoming the world standard.

When 35 mm. film is prepared for a 2 by 2 inch slide as is customary and used with a projector furnished with a 5 inch objective lens, which is the proper size for most situations, the image at 10 feet is 20 by 30 inches, but as no scanning lines are present a clear image is comfortably perceived. The trend is to larger picture tubes, and the 10 inch tube has actually been discontinued by some manufacturers.

The introduction of directional pattern in the tube has resulted in a substantial brightness gain and reduced the detrimental effects of room lighting on picture contrast. Now, even with subdued room lighting, the highlight brightnesses between 30 and 100 foot-lamberts are not productive of significant glare.

Answer.—Television is still too recent to permit definite answers to this question. However, the history of moving picture viewing may be helpful. It was the jumpy, poorly alined sequence of frames and the obvious flicker that were the disturbing factors. Patrons tried to sit far back in the theater so that the angular extent of the jumpiness was reduced. In television, while there is no problem of over-all flicker, there is the problem of the finite size of the picture structure and the repetition rate that in essence gives a sense of flicker. The more the defects in the picture, the greater is the tendency for visual fatigue. This includes such defects as out-of-focus pictures, those that are too dim, too flat and with too much contrast, and those that weave and jump. The viewing distance should therefore not be near enough for these defects, especially the graininess, to be overly apparent. This is more important than size of picture, although the graininess and size may go together. Furthermore the appearance of graininess will increase with the increase in brightness of the screen. Television should be observed in a lighted room, so that there is not too great a contrast between the screen and the background.

Answer.—The optimal distance from which one should watch television varies from one person to another, depending at least partly on his state of refraction and on the size of the screen. Placement of furniture and room size also influence one's preference. In general, a distance of 10 feet or more would be preferable, since then there is necessary only a moderate amount of convergence and accommodation. One should avoid sitting closer than 5 feet. As a general recommendation for small or moderate size screens, a distance of roughly 10 times the diameter of the screen is found most comfortable for clear viewing and avoidance of eye fatigue. If eye fatigue occurs at about this distance in a person with no visual abnormalities, the distance may be changed. In fact, changing occasionally from one chair to another should help in avoidance of fatigue not only of the sense of vision but of the neck muscles. Regardless of the distance of viewing, there seems to be no evidence that eye fatigue in the "normal" eye will cause pathological changes. The chief problem is that of comfort.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

## DETERIORATION OF PLASMA IN STORAGE

To the Editor:—*Is authentic evidence available concerning the deterioration in storage of dried plasma?*

*H. A. Folse, M.D., Donaldsonville, La.*

Answer.—Considerable evidence has been accumulated to show that deterioration of plasma is very slow when the material has been properly dried from the frozen state and stored under vacuum in sealed containers. It has been found that prothrombin and complement, both of which are very labile factors, are reasonably well preserved even after eight years (Strumia, M. M., and McGraw, J. J.: Blood and Plasma Transfusions, Philadelphia, F. A. Davis Co., 1949). Similar evidence showing excellent preservation for long periods of time for various factors contained in plasma and serum, including the specific antibodies, has also been reported (Flosdorf, E. W.; Hull, L. W., and Mudd, S.: Drying by Sublimation, *J. Immunol.* **50**:21, 1945).

Preservation of the various factors in plasma is dependent on proper preparation, proper packaging and, in some instances, on the temperature of storage. It must be dried from the frozen state to a moisture content of less than 1 per cent and stored in sealed bottles under vacuum and away from light. Storage at cold temperatures is not necessary for dried plasma, but it probably does slow the processes of deterioration even further. In the case of prothrombin activity it is necessary to dissolve the dried plasma with acidified water. This is true because the process of drying removes carbon dioxide. Redissolving with neutral distilled water results in a definite increase in the $p_H$, which decidedly decreases the prothrombin activity.

## ATMOSPHERIC HUMIDITY AND HEALTH

To the Editor:—*An air-conditioning system in an industrial plant was operating to maintain a relative humidity of 55 per cent at 75 F. What effect, if any, will the conditions have on the health of employees working in that plant?*

*C. J. Fairo, M.D., Cincinnati, Ohio.*

Answer.—There is no evidence that a relative humidity of 55 per cent with a temperature of 75 F. is prejudicial to health in the wintertime, provided that the employees take reasonable precaution in changing their moist working clothes to dry street clothes before going out into the cold. In the summertime, the indoor air condition under consideration is suitable for physical work, but the relatively low temperature may aggravate the oppressive effect of heat experienced when workers pass from the cool indoor air to the hot outdoor atmospheres. Exposure to excessive contrasts may be prevented by provision of a suitably conditioned dressing room to serve as an adjustment room for gradual adaptation of workers to the prevailing outside temperature.

Studies of the effects of high humidities on health were made by the British Industrial Fatigue Research Board (Hill, A. B.: Artificial Humidification in the Cotton Weaving Industry, Rep. 48, London, His Majesty's Stationery Office, 1927) and the U. S. Public Health Service (Britten, R. H.; Bloomfield, J. J., and Goddard, J. C.: The Health of Workers in a Textile Plant, Pub. Health Bull. 207, Washington, D. C., Government Printing Office, 1933). Both studies were carried out in cotton

weaving plants where relative humidities between 75 and 90 per cent are normally maintained. Besides discomfort, no difference in the incidence or duration of illness could be found between two large groups of men, one group working in wet sheds and the other in dry sheds.

## SHOULD THESE BOYS PLAY BASKETBALL?

To the Editor:—*Is it safe for an 18 year old boy who had a spontaneous subarachnoid hemorrhage two years ago to play basketball? He recovered without sequelae and at this time is neurologically sound.*

*Bruce C. McIntyre, M.D., St. John, Wash.*

Answer.—It is likely that the spontaneous subarachnoid hemorrhage resulted from a ruptured intracranial aneurysm. Certainly it would be inadvisable for a patient with such a lesion to engage in basketball or any other violent physical activities.

To the Editor:—*A 16 year old boy, examined June 6, 1950, had swelling of the hands and face, pitting edema of the legs, blood pressure of 150/108, a 4 plus albumin reaction and many red blood cells, white blood cells and granular casts in the urine. Apparently an infected laceration of the forearm or a sore throat had been present two or three weeks previously. Treatment instituted was bed rest and a low protein diet. After two weeks, the blood pressure decreased and edema disappeared, but the urine continued to show formed elements until the middle of August. His blood pressure did not reach normal until August 21. The sedimentation rate on July 15, 1950, was 42 mm. in one hour (Wintrobe). This boy is a potential basketball star at a high school. I have advised that he not be permitted to play the next semester. The coach has taken him to other doctors, who examined him after all physical signs of illness had disappeared. I was informed today that the boy will play basketball. What is your opinion?*

*John M. Bretz, M.D., Huntingburg, Ind.*

Answer.—Every high school athletic code places the health and welfare of players above all other considerations. Sometimes community pressures or the ambition to develop a winning team lead to unethical practice. Except in extraordinary circumstances the opinion of the family physician who treats a high school athlete and is familiar with his medical background must supersede that of a physician unacquainted with the details of the illness and the diagnosis and treatment of the attending physician. In the case cited, whether or not the boy's future health was jeopardized, the fundamental failure was the lack of established procedure for handling this kind of situation. Principal conclusion 16 of the Second National Conference on Physicians and Schools, American Medical Association, 1949, reads as follows: "When problems arise involving medical judgment in which the family physician and school physician are concerned, the customary channel of consultation with appropriate specialists to settle the issue should be used with the agreement of the family and physicians involved." Many medical societies have a committee responsible for counseling with school officials on health problems in the school. Where there appears to be a valid reason for questioning the judgment of a physician attending an athlete, the coach should request consultation. If the request is not granted, he should refer the matter to this medical society committee through the proper channels rather than seek a contrary opinion from a physician less well acquainted with the health problems of the child in question. The responsibility for the determination of the fitness of an adolescent to play is a heavy one. Coaches as well as physicians should approach these cases of doubt and differences of opinion with extreme care, not only as a means of protecting the players involved but to preserve good relation between physicians and schools. Well conducted and supervised athletic work can have real value for the participants, but no player should ever be subjected to unnecessary risks. This is particularly true for adolescent youth.

## INTESTINAL NEURITIS IN A DIABETIC

To the Editor:—*A woman aged 38 has been diabetic for 15 years. Ten to 15 units of protamine zinc insulin injection control the blood sugar level, but the patient now has diarrhea. Meals are followed by a need to evacuate at 15 to 20 minute intervals. She also has albumin following recurring attacks of pyelitis. Blood pressure is 160/85. All kinds of laboratory tests of stools have been negative. Gastric juice was tested for hydrochloric acid content and was found normal. She is nervous. What treatment would you suggest? W. H. Bollinger, M.D., Charleston, Ark.*

Answer.—Evidently this patient has hypertension and nephritis, together with diarrhea of the type frequently due to neuritis involving the innervation of the intestines. This type of diarrhea is severer at night, and often there is loss of control of the movements. If proctoscopic and roentgen examination, together with stool tests, have shown no ulceration and no evidence of colitis or infection with amebas, then treatment must be directed to the neuritis. The diet may be concentrated so that coarse vegetables and particularly salads are eliminated. Addition of cheese and boiled milk to the diet is sometimes helpful. Injections of crude liver extract, 2 to 4 cc. every other day, occasionally cause improvement. Atropine, given by injection at night in moderate doses, is beneficial. The use of vitamin B complex has been recommended. In some patients the condition persists for many months and then spontaneously improves.

## SEDIMENTATION RATE IN ARTHRITIS

To the Editor:—A 65 year old patient who has degenerative *arthritis had a sedimentation rate (Westergren) of 30 mm. in November 1949 and 45 mm. in April 1950. There are no inflammatory lesions besides the arthritis, no tuberculosis and no suspicion of cancer. Can arthritis which causes only stiffness of the knee joints, but never acute pain, be responsible for the high sedimentation rate? M.D., Iowa.*

Answer.—A sedimentation rate of 30 to 45 mm. (Westergren) would be typical of atrophic arthritis, unusual in degenerative arthritis, especially when the patient is free of acute pain. The sedimentation rate is increased in association with elevated concentration of plasma fibrinogen or serum globulin (Ham, T. H., and Curtis, F. C.: Sedimentation Rate of Erythrocytes, *Medicine* 17:447,1938). Plasma fibrinogen is the globulin that is increased regularly in inflammations, neoplastic disease and certain other conditions. Serum globulin is elevated in such conditions as multiple myeloma, chronic infections and chronic disease of the liver. It is suggested that the globulin of the serum be determined, the upper limit of normal being approximately 2.5 Gm. per 100 cc. of serum (maximum normal, 3.0 Gm.). If hyperglobulinemia is present, this may serve as a lead in diagnosis. One should make repeated observation in an attempt to define the cause of the abnormal concentration of blood proteins.

## THE PROSTHETIC EAR IN YOUNG CHILDREN

To the Editor:—*A baby was born with a deformed ear, and the parents would like to get a sponge rubber ear made until such time as the child is old enough to have plastic work done on the ear.*

*Louis H. Bos., M.D., Rehoboth, N. Mex.*

Answer.—This inquiry must be answered with some reservation, because of the injuries or congenital defects that can be associated with this type of ear deformity plus the growth potential of any remaining structures. If the child has any cartilagenous ear remnants and has an external auditory canal the possibilities of one's doing a satisfactory plastic repair, using the child's own tissues, are much enhanced. If there is no remaining structure of the ear, then, of course, the prosthetic problem is greatly increased. However, children born with congenital absence of all or part of the ear frequently have associated with it a deformity of the mandible. This may manifest itself as an asymmetry of the face, failure

of development of the ascending ramus or body of the mandible on the affected side and frequently with a deviation to the side of the defect. Some of the maldevelopment is often partially or wholly compensated for by vigorous use of the jaws in chewing and normal sucking action in infancy. It is advisable for the child to be very active in the use of the muscles of mastication and associated structures. If some auricular cartilage is present, it should be allowed to grow as much as possible because an ear can be most satisfactorily reconstructed with the use of structures that are already present. The surgical procedures that would interfere with cartilagenous growth are as a rule not instituted before the patient is 4 years of age and sometimes are deferred longer.

As to the use of a prosthetic ear or a "sponge rubber ear," it is a questionable procedure as far as a satisfactory cosmetic and functional result is concerned at the age stated. These appliances have to be held in position by adhesives or glue of some type, and the child is continually displacing them. If the child is a female, allowing the hair to grow to cover up the defect is the easiest substitute. In a male the problem is more difficult and a prosthetic ear can be utilized. However, an ear constructed of plastic material and placed over the auricular region is constantly displaced by movement of the jaw, and it is only partially satisfactory. Continuous over-all growth of the child, specifically the ear on the opposite side, particularly by comparison, means that the prosthesis has to be changed rather frequently. The color of the normal ear as it changes from season to season must also be matched with the prosthetic ear, which means that many replacements over a period of years would be necessary. Since each one of these must be sculptured and each one must have a separate mold made for it to retain the greatest amount of adhesion to whatever structures are present, it is a lengthy and expensive procedure.

It is the practice in many clinics to do nothing for these children until they have obtained as much growth as possible. This is usually complete at 4 to 6 years of age. This could be altered greatly, however, depending on the type of deformity. In general, the reconstructive procedures are started about the fourth year or as late as the sixth year and gradually accomplished; sometimes the main portion is done first, the final adjustments being deferred for a period of years. The time of any and all procedures, because of the degree of deformity and the amount of normal tissue present is extremely variable. It has been the experience in many large clinics that the prosthetic ear made of rubber or any of the synthetic plastic materials is extremely unsatisfactory in young children.

## SODIUM CYCLAMATE (SUCARYL®) AND NEPHRITIS

TO THE EDITOR:—*One is cautioned against using sodium cyclamate (sucaryl®) in the presence of kidney disease. Is this because of the sodium content? If so, what is the sodium content (in milligrams) per tablet?*

*W. F. Holmes, M.D., Walla Walla, Wash.*

ANSWER.—Sodium cyclamate contains 173 mg. of sodium per gram; the dose limitation set by the distributor is 1.5 Gm., and if patients are kept within this limit they would ingest 260 mg. of sodium or the equivalent of that contained in 660 mg. of table salt. Since low salt diets today often are held below 500 mg. of sodium chloride, or 200 mg. of sodium, sucaryl might be undesirable for cardiac, nephrotic or cirrhotic patients. In nephritis with impending uremia, rigid sodium restriction often is dangerous, since the kidney may reabsorb electrolytes poorly. In such cases sodium cyclamate would be permitted as part of a diet providing 1 to 3 Gm. of sodium chloride per day. The organic molecule is without effect on rats, fed throughout the life span on a diet containing 5 per cent of sodium cyclamate, and, like saccharin, it is freely soluble in water and readily excreted even when renal function is impaired. So far as is known it is safe to use in the low protein diets for uremic persons, but as these persons always have a high level of carbohydrate it is difficult to conceive of a situation in which its use would be recommended.

## ASPIRIN LOCALLY AFTER TONSILLECTOMY

TO THE EDITOR:—*Some physicians believe that acetylsalicylic acid (aspirin) used locally in the throat after tonsillectomy tends to cause post-tonsillectomy hemorrhage. Is there any truth in this?*

*M.D., Mississippi.*

ANSWER.—The possibility that salicylate therapy may produce hemorrhage by reduction in blood prothrombin has received some attention both clinically and experimentally. There is no convincing data showing that acetylsalicylic acid in normal persons has produced prothrombin deficiency in hemorrhagic proportions. Most workers agree that the prothrombin level must be less than 40 per cent in all persons and less than 10 per cent in some, for spontaneous bleeding to be produced. This is not caused by salicylate therapy. Aspirin used locally could possibly contribute to post-tonsillectomy hemorrhage by irritation but not through lowering of the prothrombin level.

## CHRONIC GLOMERULONEPHRITIS

TO THE EDITOR:—*A woman aged 24 was found two years ago to have albumin, casts and red blood cells in the urine. She also has had periodic attacks of chills and fever with pyuria, which at first responded to sulfonamide drugs but then was not affected by any antibiotic. The urine gradually becomes clear of the pus cells and in the intervals is normal except for casts and albumin. She had a normal intravenous pyelogram and retrograde pyelogram. There is no positive urine culture. Her blood pressure is normal, and there is no glycosuria. Renal function is normal. Would she be a candidate for measles inocculation? Would foreign protein (typhoid) be helpful? Has pituitary adrenocorticotropic hormone (ACTH) or cortisone been used? I would appreciate your suggestions for treatment other than the normal nephritic routine.*

*Hugh S. Brown, M.D., Spokane, Wash.*

ANSWER.—While leukocytes in the urine in excess are not uncommon in active glomerulonephritis, chills and fever with pyuria point strongly to pyelonephritis or lower urinary tract infection. However, negative urine cultures are unusual, although they have been reported in cases of so-called abacterial, possibly virus, pyuria. Urine cultures should be repeated after chemotherapy has been discontinued for some time. Certainly tuberculosis should be excluded by appropriate culture and guinea pig inoculation of the concentrated urinary sediment. The rare possibility of the urinary findings and episodes of fever being part of a diffuse collagen disease should be considered. The most likely diagnosis is chronic glomerulonephritis with a superimposed urinary tract infection.

There is no indication for inoculation with measles, since the patient does not have a nephrotic syndrome and is not in the proper age group. Foreign protein therapy is of no value. Pituitary adrenocorticotropic hormone and cortisone have been used with temporary success in the nephrotic stage of glomerulonephritis. It is doubtful whether they would produce any permanent effect on proteinuria. They could be tried on a purely experimental basis. Nitrogen mustard has been used experimentally with some success in a small series of patients with acute and subacute glomerulonephritis in an attempt to suppress antibody formation allegedly responsible for the continuation of the renal inflammation. This is not recommended for general use.

## BUERGER'S DISEASE

TO THE EDITOR:—*A 62 year old man has been given a diagnosis of Buerger's disease; please outline treatment. Is insulin effective in the treatment of Buerger's disease?*

*M.D., Montana.*

ANSWER.—If the onset of the symptoms occurred within the past 10 years, the diagnosis of Buerger's disease is almost certainly incorrect since this is a young man's disease; it rarely originates after the age of 50 and never, so far as is known,

after the age of 60. It is frequently confused with arteriosclerosis obliterans in older men, and it seems likely that this applies to the present case. Treatment depends on the degree of involvement of the arteries, the presence or absence of open ulcers or gangrene and other factors. It may include cessation of smoking, reflex heat with elevation of the head of the bed and vasodilating substances. Insulin, along with numerous other recently suggested measures, has not been established to be of value except when indicated because of the presence of diabetes mellitus. For more complete discussions of this and allied conditions, the reader is referred to the following books: Vascular Diseases in Clinical Practice by I. S. Wright (Chicago, The Year Book Publishers, Inc., 1948) and Peripheral Vascular Diseases by Allen, Barker and Hines (Philadelphia, W. B. Saunders Company, 1946).

## RAW POTATOES

To the Editor:—*I have a patient that is fond of eating raw potatoes. He claims that the food value is the same whether eaten raw or cooked. Is this statement true? Is there any danger of one's eating too many raw potatoes?*

*Harold M. Hoover, M.D., Joliet, Ill.*

Answer.—The food value of raw potato cannot be determined by simple food analysis. From the laboratory analysis the food value of raw potatoes would be higher than that of the cooked ones in an amount that would depend, chiefly, on the cooking losses of ascorbic acid and thiamine. When, however, the comparative nutritive value to the patient is the consideration, the question of digestibility becomes paramount. Potatoes are a low fibered, low protein vegetable, high in starch. When potatoes are cooked, they are highly digestible and frequently almost completely digested before they leave the stomach. Equivalent digestion experiments on raw potatoes are not available. Digestion tests on raw starches have been made. In these tests, healthy men appeared to digest as much as 100 Gm. of raw wheat or corn starch combined with milk at a meal, but when raw potato starch was fed in the same manner, 20 to 40 per cent of it appeared in the feces. In one study with the potato starch, "flatulence usually accompanied by cramplike pain was a prominent and distressing symptom in all the subjects." The amount of starch used in these experiments would seem to be maximum, and to duplicate it would require the consumption of four to five medium-sized potatoes.

Briefly, then, raw potatoes contain more ascorbic acid and thiamine than cooked potatoes, while cooked potatoes probably provide more available energy than raw potatoes. Four to five medium-sized raw potatoes are likely to be too many at one time for most persons. If one to two raw potatoes can be eaten without resulting flatulence or other discomfort, they are probably at least moderately well digested.

## CHRONIC MYELOGENOUS LEUKEMIA

To the Editor:—*Chronic myelogenous leukemia developed in a 40 year old man. He had been taking potassium thiocyanate for a period of two years in large dosage without medical supervision, the medicament being taken for essential hypertension. Have you any records of possible association between potassium thiocyanate and leukemia? Could there be a hemopoietic stimulating effect causing proliferation of the myeloid elements, thus starting the leukemic process?*

*M.D., West Virginia.*

Answer.—There are many published evidences of toxic reactions from potassium thiocyanate used therapeutically or in suicidal intents, but the only known hematological effects are leukopenia, anemia, thrombocytopenia or leukemoid reactions. There are no reported incidences of chronic myelogenous leukemia or any other type of leukemia following the use of the drug. It is conceivable that in the case cited the stimulus of the hemopoiesis through the toxic agent (potassium thiocyanate) may have upset the leukemia in its latent or asymptomatic state and caused a rapid progression of the process in the development of a definite clinical leukemic picture.

## RESISTANCE OF TUBERCLE BACILLI TO HEAT

To the Editor:—*What is the thermal death point of Mycobacterium tuberculosis heated for 10 minutes and the thermal death time in the presence of moisture at 100 C.? What would be the best method for determining whether cooking utensils, such as aluminum pots, are free of Mycobacterium tuberculosis? Since the culture of these organisms is slow, could the destruction of some other organism, such as Escherichia coli, be used as indicative of proper sterilization?*

*Edward W. Gray, M.D., West Brentwood, N. Y.*

Answer.—The thermal death point of the Mycobacterium tuberculosis (var. human) heated for 10 minutes in pure suspension in a buffer medium is about 70 C. (Corper, H. J., and Cohn, M. L.: The Thermolability of the Tubercle Bacillus, *Am. Rev. Tuberc.* **35**:663-677, 1937; and Corper, H. J., and Cohn, M. L.: Some Fundamental Investigations on the Resistance of Tubercle Bacilli, *J. Bact.* **35**:223-233, 1938). However, under certain conditions, they may survive at 80 C. for 10 to 40 minutes (Larmola, E.: *Ueber die Hitzeempfindlichkeit der Tuberkelbazillen, Zentralbl. f. Bakt.* [*Abt. 1*] **151**:48-50, 1943). The thermal death time for moist bacilli at 100 C. is a few minutes. In contrast, dried bacilli can resist even autoclaving at 118 C. in a sealed tube. This, therefore, must be considered in any specific instance involving the killing of the bacilli, for there are two factors that account for the variable figures recorded as the thermal death point. For successful destruction of the bacilli, heat must penetrate and moisture is necessary. Thus, the question of sterilization of eating utensils, and, specifically, aluminum pots, is tempered by the time when these pots or eating utensils reach the critical lethal temperature. Obviously a rapid dip in boiling water may fail to destroy the bacilli, whereas complete submersion for 10 minutes, with sufficient time for thorough heating of the utensil, may destroy the bacilli, unless they are embedded in a nonconducting, heat-resistant material. The cultural disclosure of viable tubercle bacilli (or guinea pig inoculation), though slow, can now be performed readily and is the only direct criterion for determining their presence in viable form. No substitute micro-organisms can yield accurate information on the survival of mammalian tubercle bacilli, because of the unique and individual characteristics of this Mycobacterium. The destruction of E. coli thus would be no index.

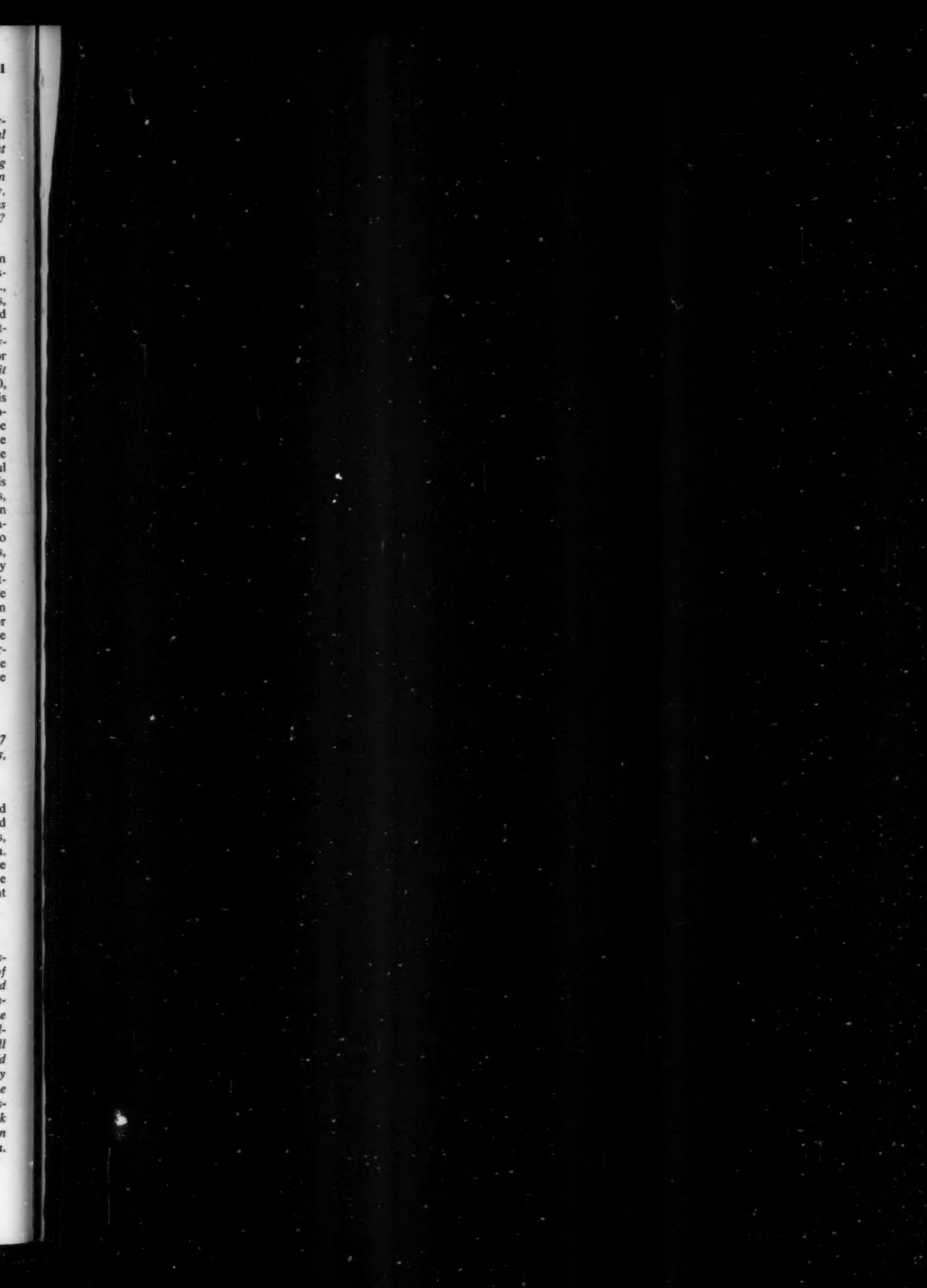
## EXCESSIVE SALIVATION

To the Editor:—*What can cause profuse salivation in a 27 month old girl whose mouth, teeth, swallowing faculties, mind and thyroid appear normal?*

*Arthur M. Dougherty, M.D., Dodge City, Kan.*

Answer:—Excess salivation, or ptyalism, in a 27 month old girl whose mouth, teeth, swallowing faculties, mind and thyroid appear normal may be caused by intestinal parasites, mercury poisoning, scurvy, hyperchlorhydria or cretinism. However, one must distinguish between the actual increase in the amount of salivary excretion and pseudoptyalism, the apparent accumulation or dribbling of the normal amount of saliva.

## SEXUAL AGGRESSION FOLLOWING VASECTOMY

To the Editor:—*The answer to the query "Sexual Aggression Following Vasectomy" in the October 21 issue of* The Journal *was of special interest to me as I have had occasion to observe the effect of vasectomy in several hundreds of cases. I fully agree with the answer that excessive sexual reactions have not been observed immediately following the operation. Increased libido, however, as well as a greater readiness for erection have indeed occurred rather frequently. I believe that such reaction is not entirely psychological but may well be due to a direct endocrine effect from the operation. The ligation of the vas ("vasectomy" being usually "vasoligation") can produce back pressure into the testis. This in turn may lead to a sudden outpouring of testicular hormone and consequent erotization.*

*Harry Benjamin, M.D.*